volume 22
number 11
november 1961

DEC 11 1961

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

Diseases *of the* Nervous System

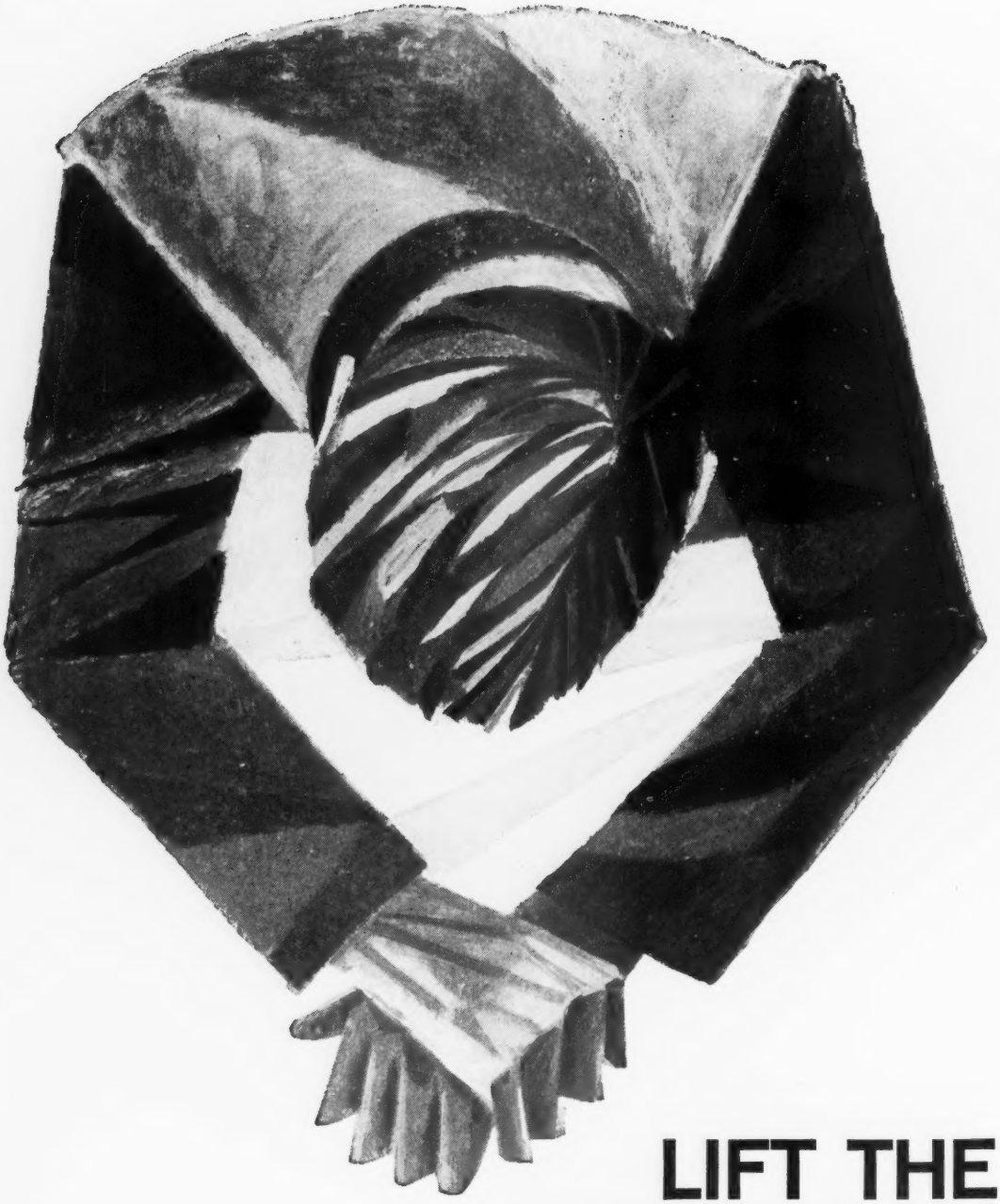
A Practical Journal on Psychiatry and Neurology

(CONTENTS ON PAGE 594)

Published Monthly by

PHYSICIANS POSTGRADUATE PRESS
277 Broadway - New York 7, New York

Entered as second-class matter at
the Post Office at New York, N. Y.



LIFT THE DEPRESSION

Lift the depression with Marplan. Marplan has been shown to be considerably more potent than certain other amine oxidase regulators. While clinically such increase in potency has heretofore been associated with increased side effects, Marplan strikes a happy balance of potency/safety. Marplan has shown markedly fewer of the side reactions of the hydrazines (such as orthostatic hypotension, constipation, jitteriness, peripheral edema, skin rash). Moreover, throughout the extensive clinical investigations, no liver damage has been reported. Marplan is an amine oxidase regulator, however, and like all of these agents, it is contraindicated in the presence of liver or kidney disease.

Indications range from moderate to severe psychiatric disorders with associated symptoms of depression, withdrawal or regression. Marplan is also valuable as an adjunct in psychotherapy to facilitate the patient's responsiveness. *Complete literature* giving dosage, side effects and precautions is available upon request and should be consulted before prescribing.

Supplied: 10-mg tablets in bottles of 100 and 1000.

Bibliography: **1.** H. F. Darling, W. Kruse, C. F. Hess and M. G. Hoermann, *Dis. Nerv. System, 20*:269, 1959. **2.** G. C. Griffith, *Clin. Med., 6*:1555, 1959. **3.** R. B. Ford, H. E. Branham and J. J. Cleckley, *ibid.*, p. 1559. **4.** H. Azima, H. Durost, D. Arthurs and A. Silver, *Am. J. Psychiat., 116*:453, 1959. **5.** L. Alexander and S. R. Lipsett, *Dis. Nerv. System, 20*:(Suppl.), 26, 1959. **6.** H. F. Darling, *Am. J. Psychiat., 116*:355, 1959. **7.** A. L. Scherbel and J. W. Harrison, *Ann. New York Acad. Sc., 80*:(Art. 3), 820, 1959. **8.** L. O. Randall and R. E. Bagdon, *ibid.*, p. 626. **9.** G. Zbinden and A. Studer, *ibid.*, p. 873. **10.** O. Resnick, *ibid.*, p. 726. **11.** T. R. Robie, *Dis. Nerv. System, 20*:182, 1959. **12.** A. Feldstein, H. Hoagland and H. Freeman, *Science, 130*:500, 1959. **13.** L. O. Randall and R. E. Bagdon, *Dis. Nerv. System, 19*:539, 1958. **14.** W. Hollander and R. W. Wilkins, in J. H. Moyer, Ed., *Hypertension*, Philadelphia, W. B. Saunders Co., 1959, p. 399. **15.** I. Kimbell and A. Pokorny, paper read at Symposium on Newer Antidepressants and Other Psychotherapeutic Drugs, Galveston, Texas, Nov. 13-14, 1959. **16.** D. Goldman, *ibid.* **17.** J. E. Oltman and S. Friedman, *ibid.* **18.** G. Zbinden, *ibid.* **19.** G. C. Griffith and R. W. Oblath, *ibid.* **20.** H. Freeman, *ibid.* **21.** W. B. Abrams, A. Bernstein, V. D. Mattia, Jr., R. J. Floody and L. O. Randall, Scientific Exhibit, American Medical Association Meeting, Atlantic City, N. J., June 8-12, 1959. **22.** R. W. Oblath, paper read at American Therapeutic Society, 60th Annual Meeting, Atlantic City, N. J., June 6, 1959. **23.** S. L. Cole, *ibid.* **24.** I. Kimbell, Jr., paper read at Cooperative Chemotherapy Studies in Psychiatry, 4th Annual Research Conference, Memphis, Tenn., May 20-22, 1959. **25.** L. O. Randall and R. E. Bagdon, Second Marsilid Symposium, Chicago, May 8, 1958. **26.** W. B. Abrams, D. W. Lewis and M. C. Becker, paper read at the International Symposium on Catecholamines in Cardiovascular Pathology, Burlington, Vt., Aug. 23-26, 1959. **27.** H. I. Russek, *Angiology*, to be published.

MARPLAN®—brand of isocarboxazid

Marplan

ROCHE
LABORATORIES
Division of
Hoffmann-La Roche Inc.

Volume XXII NOVEMBER 1961 Number 11

DISEASES *of the* Nervous System

Contents

RECENT DEVELOPMENTS IN PSYCHOSOMATIC RESEARCH 609
Robert B. White

CHANGES IN AGE DISTRIBUTION OF A SCHIZOPHRENIC POPULATION 616
G. Donald Niswander and George M. Haslerud

SPECTROGRAPHIC AND CHROMATOGRAPHIC STUDIES IN PSYCHOTICS AS INFLUENCED BY EST 619
Thomas M. Runge, Sidney W. Bohls, Sam A. Hoerster, Jr., and Nawasa Thurman

TWO NEW BUTYROPHENONE DERIVATIVES STUDIED WITH THE CONDITIONED REFLEX TECHNIQUE 623
G. F. Golwurm and F. Vanni

ANOREXIA NERVOSA: TREATMENT WITH HYPNOSIS AND ECT 627
Harry K. Davis

PSYCHIATRIC OBSERVATIONS ON JUVENILE DELINQUENTS IN RESIDENTIAL TREATMENT 632
Selwyn Brody

EFFECT OF CHLORPROTHIXENE ON SCHIZOPHRENIC PATIENTS 636
Albert A. Kurland and Esber Yazicioglu

A CLINICAL TRIAL STUDY OF TRIFLUOPERAZINE 639
Nina Kateryniuk and Charles W. Morris

AN UNUSUAL REACTION TO AN MAO INHIBITOR 641
J. Tupin

EASTERN PSYCHIATRIC RESEARCH ASSOCIATION 645

AN ORGANIZATION OF EX-PATIENTS OF A PSYCHIATRIC HOSPITAL 645
Jacob H. Friedman

BOOK REVIEWS 649

EDITOR
Titus H. Harris, M.D. 112 North Boulevard, Galveston, Texas

MANAGING EDITOR
George Bisgeir, B.S., LL.B. New York, New York

ASSOCIATE EDITORS

A. F. Bennett, M.D.----Berkeley, California
Francis J. Braceland, M.D.----Hartford, Conn.
Franklin G. Ebaugh, M.D.----Denver, Colorado
Hamilton Ford, M.D.----Galveston, Texas
Walter Freeman, M.D.----Los Altos, California
A. Hauser, M.D.----Houston, Texas
David J. Impastato, M.D.----New York, N. Y.
Louis J. Karnosh, M.D.----Cleveland, Ohio
Frank H. Luton, M.D.----Nashville, Tennessee
Wm. Malamud, M.D.----Boston, Mass.
Karl A. Menninger, M.D.----Topeka, Kansas
Hans H. Reese, M.D.----Madison, Wisconsin
Lewis J. Siegal, M.D.----New York, New York
Harry C. Solomon, M.D.----Boston, Mass.
S. Bernard Wortis, M.D.----New York, N. Y.

YEARLY SUBSCRIPTION $10.00
Foreign Subscription $11.50

for rapid control of acute emotional disturbances:

new LIBRIUM injectable

Librium, in 100-mg ampuls, is now available for parenteral administration. Librium Injectable provides prompt symptomatic relief of alcoholic agitation, delirium tremens, hallucinosis, schizophrenic motor excitement, agitated depression, paranoid reactions and drug withdrawal reactions. The parenteral route may be preferred for rapid control of acute anxiety, hyperactivity, hysteria, phobia and panic reactions, or other acute emotional disturbances where oral administration is impractical.

Consult literature and dosage information, available on request, before prescribing.

LIBRIUM® Hydrochloride – 7-chloro-2-methylamino-5-phenyl-3H-1,4-benzodiazepine 4-oxide hydrochloride

ROCHE
LABORATORIES Division of Hoffmann-La Roche Inc.

AN OFFICIALLY APPROVED INSTRUMENT
WHICH HAS ALSO WON POPULAR APPROVAL.

the REITER MOL-AC II

for

UNEQUALLED EASE OF OPERATION

in

A.C. SHOCK THERAPY

SAFE

The MOL-AC II, provides the highest degree of complete electrical isolation, by far exceeding official code requirements, to assure the maximum in safe operation.

EFFECTIVE

Clinical results have been uniformly excellent. Side effects are automatically reduced. The MOL-AC II is acclaimed internationally by leading physicians and institutions.

AUTOMATIC

The MOL-AC II provides a highest initial current to initiate seizure pattern with an automatic reduction to safe low voltage in every case. Instantly and automatically re-set for repeated treatments. With the MOL-AC II, doctors report they are now certain of full seizure each treatment even with large doses of muscle relaxants.

EASY TO USE

Controls are simplified — one 3-position current intensity dial and one treatment switch. Just plug in ordinary AC current and the MOL-AC II is ready for immediate use. The MOL-AC II has a handsome walnut case. Attractively priced at $100.00 complete with finest physician's bag of genuine leather and attachments.

DURABLE

Ingenious design with only one moving part. Remarkable freedom from service requirement.

Also available—Reiter Model SOS, the advanced, most efficient instrument combining the strongest convulsive UNIDIRECTIONAL currents with powerful yet gentle sedative currents. (Many additional features included.) Literature on request.

REUBEN REITER, Sc.D. 64 WEST 48th ST., NEW YORK 36, N. Y.

TABLETS

INJECTION

FOR YOUR PATIENT WITH DEPRESSION

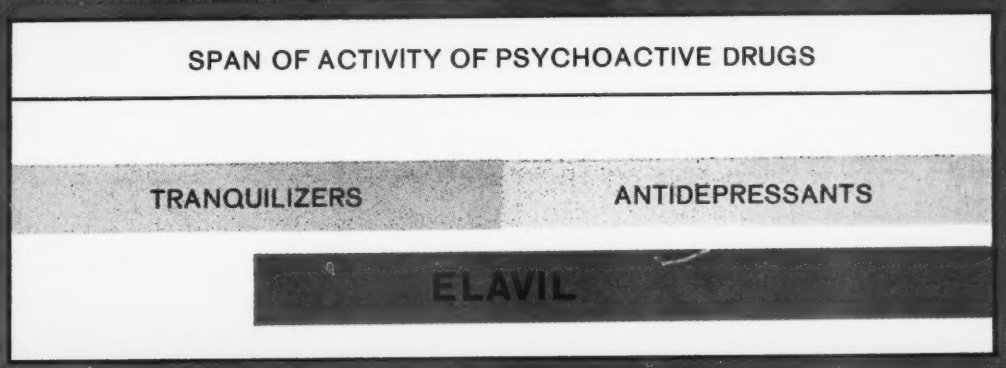
ELAVIL

AMITRIPTYLINE HYDROCHLORIDE

the antidepressant with a significant difference:

• given orally or parenterally, ELAVIL provides PROMPT relief of associated anxiety, tension, and insomnia • followed by control* of underlying depression

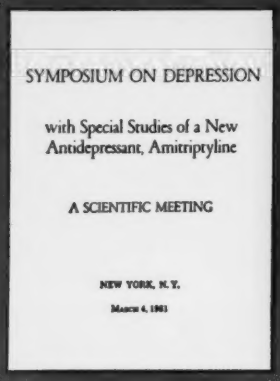
*Some depressed patients respond within 5 to 10 days, while others may require up to two weeks or longer to obtain benefit.



- a single agent (not a combination of compounds)
- effective in all types of depression...particularly useful in depressed patients with predominant symptoms of anxiety and tension
- may be used in ambulatory or hospitalized patients
- not an amine oxidase (MAO) inhibitor

MSD

please turn page for EXCERPTS FROM A SYMPOSIUM ON DEPRESSION



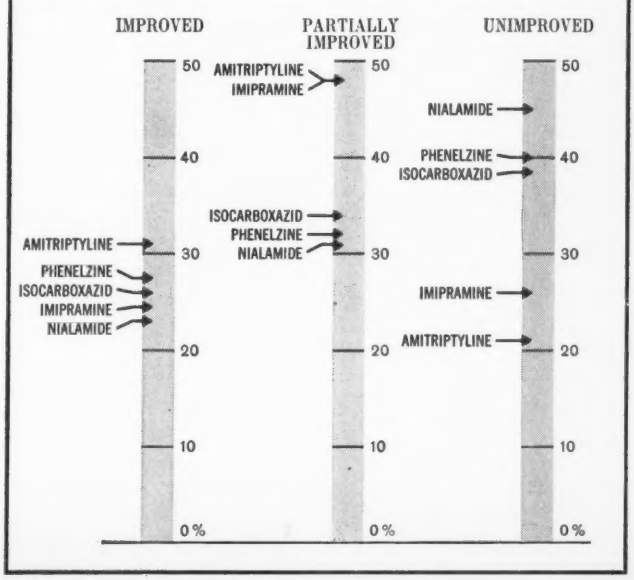
EXCERPTS FROM A SYMPOSIUM ON DEPRESSION

ELAVIL

AMITRIPTYLINE HYDROCHLORIDE

INVESTIGATOR	FINDINGS
DUNLOP, EDWIN: The treatment of depression in private practice.	"Amitriptyline [ELAVIL] has a specific advantage over any antidepressant currently available and I see increasing evidence of its usefulness in reducing tension, agitation and anxiety, as well as in relieving the depressive quality of the illness. Amitriptyline appears ... to combine better than any other antidepressant drug the successful treatment of anxiety at one end of the scale and depression at the other. Experience in the past has shown us that, when using electroshock or analeptics, although depression can be relieved, the accompanying anxiety eventually proves more troublesome than the depressive phase of the illness. Amitriptyline successfully bridges these divergent symptoms which are displayed in varying proportions in all depressive syndromes. "... Approximately one hundred and twenty patients have been studied with amitriptyline during the last fifteen months. It is an effective antidepressant when employed in both hospital and ambulatory patients. Its dependability and freedom from toxicity and severe side effects merit further evaluation on a broader spectrum of depressive disorders."
BENNETT, DOUGLAS: Treatment of depressive states with amitriptyline.	"In those cases showing a good response, early and dramatic improvement in sleeplessness resulted and many patients noted a feeling of relaxation. The ability of some patients to reduce their night sedatives after only a month's treatment was unique in my experience of the treatment of depression."
SAUNDERS, JOHN C.: Antidepressives: the pith of affective therapy.	"Its primary action in hospitalized psychotics is antidepressive; this along with its very low rate of side actions make it a drug of potentially frequent application in a broad spectrum of neuropsychiatric diseases.... Since a large part of any hospital population will reach a plateau if given only a tranquilizer or an energizer, we suggest that amitriptyline alone be given prior to combination therapy, as this drug is easier and safer to administer and produces a significant improvement in a high percentage of cases (60-75)."
OSTFELD, ADRIAN M.: Effects of an antidepressant drug on tests of mood and perception.	"Finally, it appears that amitriptyline in the doses employed here is relatively effective in depressed states of neurotic proportions. Its freedom from severe side effects in doses that are therapeutically effective seems established in this patient population."

(This symposium was published in Diseases of the Nervous System, Volume 22, Section Two—Supplement, May 1961)

INVESTIGATOR	FINDINGS
AYD, FRANK J., JR.: A critique of antidepressants.	"Amitriptyline and imipramine induce similar side effects but, generally speaking, those of amitriptyline cause less subjective discomfort in patients than those of imipramine. "... Many of the factors that favor a satisfactory response to these drugs are also those clinically associated with the expectation of a good reaction to ECT. The danger lies in their general slowness in taking effect which makes their use hazardous for severely depressed suicidal patients who, preferably, should be treated with electroshock therapy. Otherwise, these compounds can be a satisfactory substitute for shock therapy for most depressed patients. Thus, these drugs have lessened the need for ECT. On those occasions when ECT is necessary, if the shock therapy is combined with an antidepressant, ECT can be dispensed with after a few treatments." COMPARISON OF THERAPEUTIC RESULTS WITH VARIOUS ANTIDEPRESSANTS 

MSD please turn page

EXCERPTS FROM A SYMPOSIUM ON DEPRESSION (continued)

ELAVIL

AMITRIPTYLINE HYDROCHLORIDE

INVESTIGATOR	FINDINGS
DORFMAN, WILFRED: Masked depression.	"In evaluating the effectiveness of amitriptyline in all these different settings, it was considered to be effective in 17 of the 25 patients (68%)."
FELDMAN, PAUL E.: Psychotherapy and chemotherapy (amitriptyline) of anergic states.	"Compared to other energizer compounds, particularly the hydrazines, amitriptyline appears to be relatively nontoxic. The laboratory reports for the most part remained within normal limits. Occasionally, abnormal readings were reported, but these appeared only sporadically and were not related to any clinical findings."

INDICATIONS: manic-depressive reaction—depressed phase; involutional melancholia; reactive depression; schizoaffective depression; neurotic-depressive reaction; and these target symptoms: anxiety; depressed mood; insomnia; psychomotor retardation; functional somatic complaints; loss of interest; feelings of guilt; anorexia. May be used whether the emotional difficulty is a manifestation of neurosis or psychosis,[1] and in ambulatory or hospitalized patients.[1,2,3]

USUAL ADULT DOSAGE: Tablets – initial dosage 25 to 50 mg. three times a day, depending on body weight, severity, and clinical disturbances. Dosage may be adjusted up or down depending upon the response of the patient. Some patients improve rapidly, although many depressed patients require four to six weeks of therapy before obtaining antidepressant response. For the ambulatory patient the dosage range for Tablets ELAVIL is 40 to 150 mg. daily. In the hospitalized patient, a daily dosage up to 300 mg. may be required. Injection ELAVIL may be given IM to rapidly calm depressed patients with symptoms of anxiety and tension while instituting therapy of the underlying depression. Initial therapy is 2 to 3 cc. (20 to 30 mg.) IM, q.i.d.

The natural course of depression is often many months in duration. Accordingly, it is appropriate to continue maintenance therapy for at least three months after the patient has achieved satisfactory improvement in order to lessen the possibility of relapse, which may occur if the patient's depressive cycle is not complete. In the event of relapse, therapy with ELAVIL may be reinstituted.

ELAVIL is not a monoamine oxidase (MAO) inhibitor. It does, however, augment or may even potentiate the action of MAO inhibitors. Thus, in patients who have been receiving MAO inhibitors, ELAVIL should be instituted cautiously after the effects of the MAO inhibitors have been dissipated. No evidence of drug-induced jaundice, agranulocytosis, or extrapyramidal symptoms has been noted. Side effects with ELAVIL are seldom a problem and are not serious. They are dosage-related and have been readily reversible. Side effects (drowsiness, dizziness, nausea, excitement, hypotension, fine tremor, jitteriness, headache, heartburn, anorexia, increased perspiration, and skin rash), when they occur, are usually mild. However, as with all new therapeutic agents, careful observation of patients is recommended. As with other drugs possessing significant anticholinergic activity, ELAVIL is contraindicated in patients with glaucoma, prostatic hypertrophy and urinary retention.

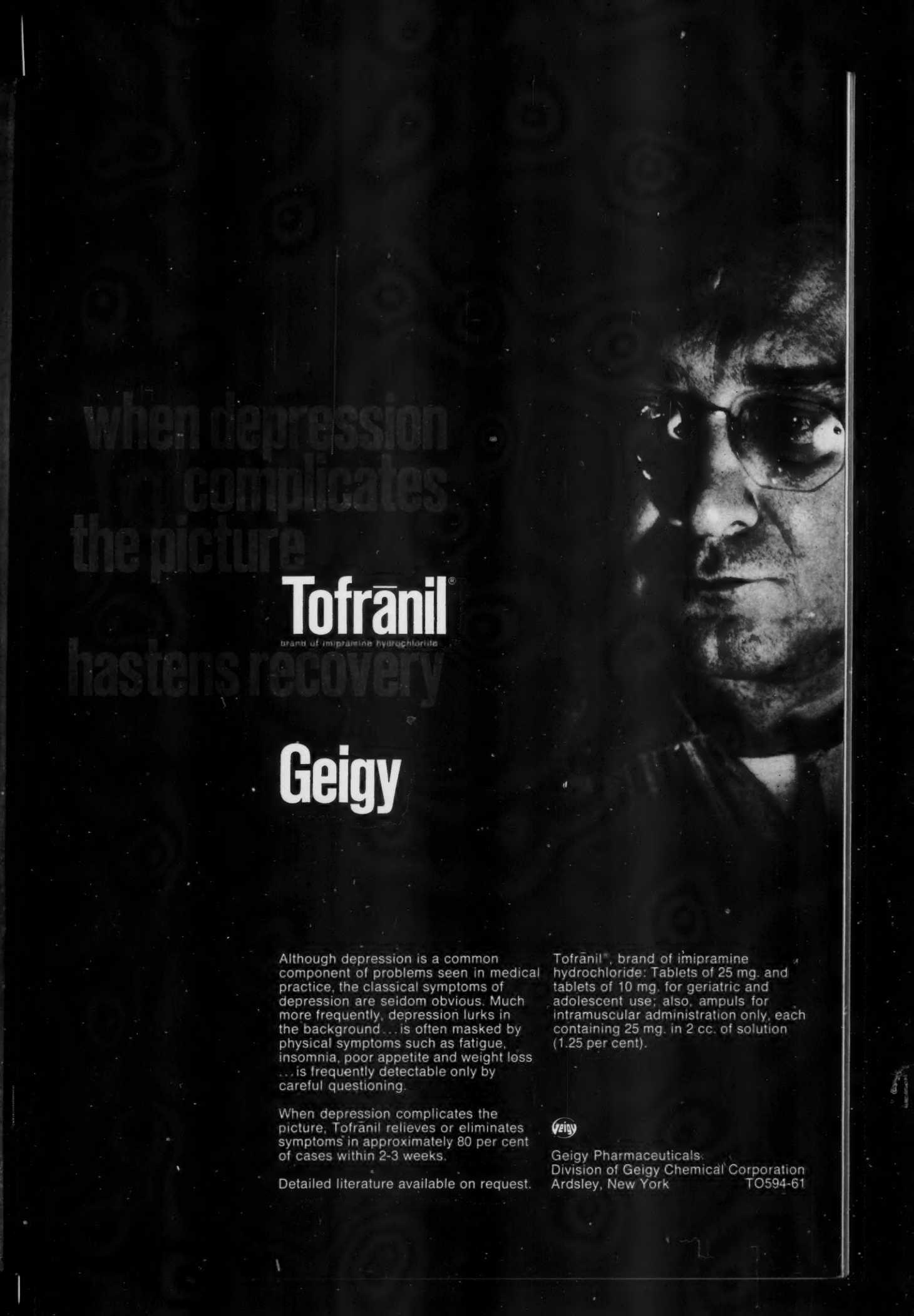
SUPPLY: Tablets, 10 mg. and 25 mg., in bottles of 100 and 1000. **Injection (intramuscular),** in 10-cc. vials, each cc. containing 10 mg. amitriptyline hydrochloride, 44 mg. dextrose, 1.5 mg. methylparaben, 0.2 mg. propylparaben, and water for injection q.s.

REFERENCES: 1. Ayd, F. J., Jr.: Psychosomatics 1:320, Nov.-Dec. 1960. 2. Dorfman, W.: Psychosomatics 1:153, May-June 1960. 3. Barss, J. A., and Saunders, J. C.: Am. J. Psychiat. 117:739, Feb. 1961.

Before prescribing or administering ELAVIL, the physician should consult the detailed information on this accompanying the package or available on request.

MSD MERCK SHARP & DOHME, DIVISION OF MERCK & CO., INC., WEST POINT, PA.

ELAVIL IS A TRADEMARK OF MERCK & CO., INC.



Although depression is a common component of problems seen in medical practice, the classical symptoms of depression are seldom obvious. Much more frequently, depression lurks in the background . . . is often masked by physical symptoms such as fatigue, insomnia, poor appetite and weight loss . . . is frequently detectable only by careful questioning.

When depression complicates the picture, Tofranil relieves or eliminates symptoms in approximately 80 per cent of cases within 2-3 weeks.

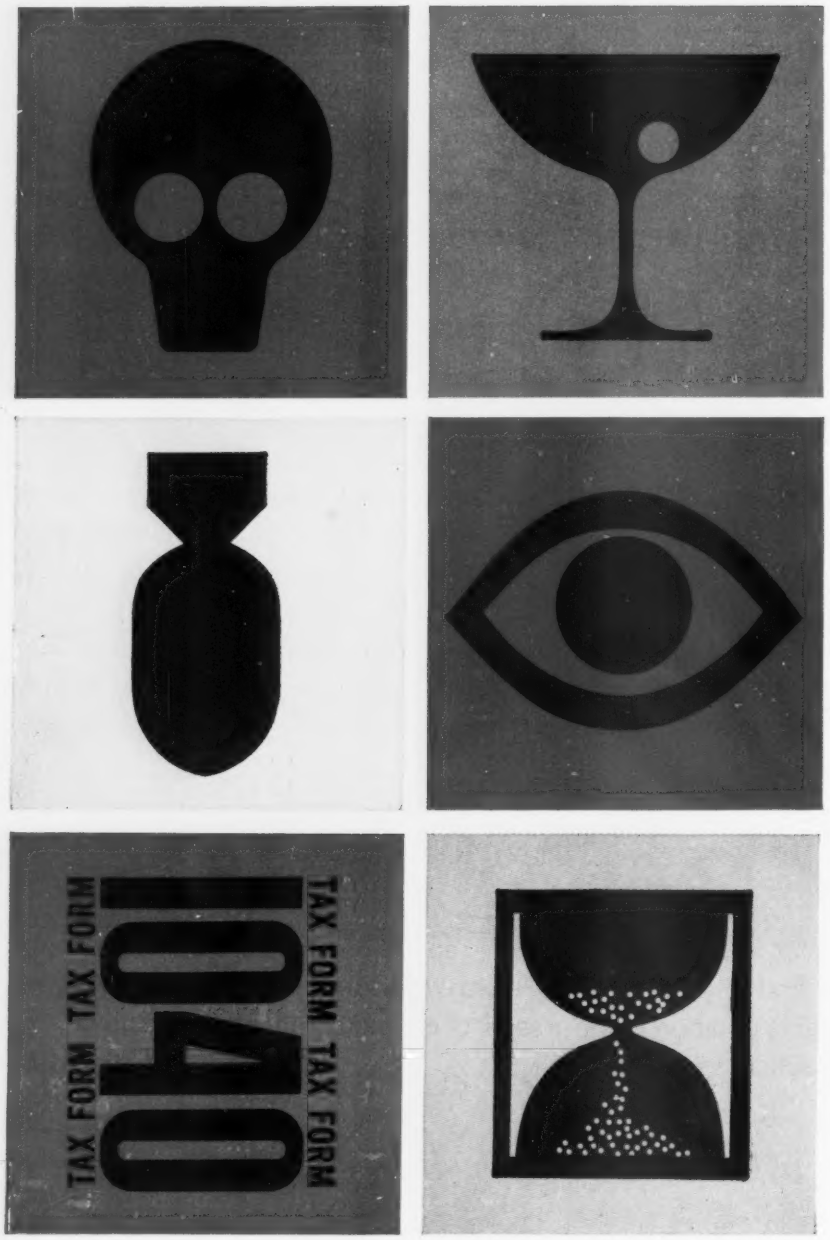
Detailed literature available on request.

Tofranil®, brand of imipramine hydrochloride: Tablets of 25 mg. and tablets of 10 mg. for geriatric and adolescent use; also, ampuls for intramuscular administration only, each containing 25 mg. in 2 cc. of solution (1.25 per cent).

Geigy Pharmaceuticals
Division of Geigy Chemical Corporation
Ardsley, New York TO594-61

ANNOUNCING THE FIRST

Symbols of the Age of Tension/Anxiety



LISTICA by ARMOUR

allays TENSION/ANXIETY...
maintains acuity... promotes eunoia*...
facilitates somatic diagnosis and therapy

SELECTIVE TENSITROPIC

LISTICA®

lifts the facade of TENSION/ANXIETY New Listica allays tension/anxiety in as many as 89% of cases,[2-13] by selectively inhibiting impulses through internuncial pathways of the central nervous system. Whether the patient's tension/anxiety is psychosomatic or a complication of somatic disorder, Listica reduces or eliminates the excess impulsivity seen in tension/anxiety states.

maintains normal acuity Unlike many drugs, Listica does not affect unconditioned response or normal motor activity. Thus, Listica allays tension and anxiety without inducing apathy or impairing acuity; patients are able to pursue normal activities, such as driving, reading, writing, etc., without interference from drug therapy.

enhances physician-patient rapport As it removes tension/anxiety, fear and frustration, **LISTICA PROMOTES EUNOIA***—"a normal mental state." It bares the patient's true somatic condition, and facilitates diagnosis and therapy. Patients are more tractable to concomitant drug therapy, respond better, faster.

without known toxicity or contraindications Listica is safe, as well as effective. Chronic studies[14] in rats (12 months) and dogs (6 months) were free of toxic manifestations at oral dosage levels as high as 200 mg./kg./day (approximately 10 times the recommended human dosage). No macroscopic or microscopic changes in tissues, organs or blood indicative of toxicity were observed, even at doses up to 320 mg./kg. In humans, there have been no adverse blood, urine or cardiac changes; liver profiles were negative, and jaundice has not been noted.

without serious side effects or habituation During three and one-half years of clinical study in 1,759 patients,[2-13] Listica has produced no serious side effects. Less than 4% of patients experienced any side effects, and these were invariably minor and transient. Most frequent (38 cases) was mild drowsiness, which disappeared after the first few days of Listica therapy. Habituation, cumulative effects, or withdrawal symptoms have not been noted, even in patients taking Listica as long as two years.

with convenient dosage and availability One Listica tablet, q.i.d., is the recommended dosage. Listica is supplied in bottles of 50 tablets on prescription only, by pharmacies everywhere. Each tablet contains 200 mg. of Hydroxyphenamate, Armour.

References:

[1]Bastian, J. W.: Classification of CNS Drugs by a Mouse Screening Battery. To be published in Intern. Arch. de Pharmacodynamie; [2]Hubata, J. A., and Hecht, R. A.: Review of Clinical Use of Hydroxyphenamate (Listica) in 1,759 Patients. To be published in Clinical Medicine; [3]Taub, S. J.: Management of Anxiety in Allergic Disorders—New Approach. To be published in Psychosomatics; [4]Cahn, B.: Experience with a New Tranquilizing Agent (Hydroxyphenamate). *Ibid;* [5]Alexander, L.: Effect of Hydroxyphenamate on Conditional Psychogalvanic Reflex in Man. Supplement to Diseases of the Nervous System, Sept., 1961; [6]Cahn, B.: Effect of Hydroxyphenamate in Treatment of Mild and Moderate Anxiety States. *Ibid;* [7]Cahn, M. M., and Levy, E. J.: Use of Hydroxyphenamate (Listica) in Dermatological Therapy. *Ibid;* [8]Davis, O. F.: On Use of Hydroxyphenamate in Anxiety Associated with Somatic Disease. *Ibid;* [9]Eisenberg, B. C.: Amelioration of Allergic Symptoms with a New Tranquilizer Drug (Listica). *Ibid;* [10]Friedman, A. P.: Pharmacological Approach to Treatment of Headache. *Ibid;* [11]Greenspan, E. B.: Use of Hydroxyphenamate in Some Forms of Cardiovascular Disease. *Ibid;* [12]Lunde, F., Davis, J., and Gouldmann, C.: Clinical Trial of Hydroxyphenamate in Alcoholic Patients. *Ibid;* [13]McLaughlin, B. E., Harris, J., and Ryan, F.: Double Blind Study Involving "Listica," Chlordiazepoxide, and "Placebo" as Adjunct to Supportive Psychotherapy in Psychiatric Clinic. *Ibid;* [14]Bastian, J. W.: Pharmacology and Toxicology of Hydroxyphenamate. *Ibid;* [15]Bossinger, C. D.: Chemistry of Hydroxyphenamate. *Ibid.*

ARMOUR PHARMACEUTICAL COMPANY, KANKAKEE, ILLINOIS

Physicians who prefer generic names prescribe "Hydroxyphenamate, Armour."

LISTICA—Hydroxyphenamate, Armour. ©1961, A.P. CO. *Stedman's Medical Dictionary

alone, depressed, and anxious
"...with no language but a cry."
Alfred, Lord Tennyson

Nardil, a true antidepressant, will help lift the depressive state and bring your patients into better contact with reality so that they may begin to accept and deal with the requirements of psychotherapy. Full dosage information, available on request, should be consulted before initiating therapy.

WARNER CHILCOTT
MORRIS PLAINS, N.J.

Nardil®

brand of phenelzine dihydrogen sulfate
A TRUE ANTIDEPRESSANT

MEDICAL LIBRARY
HISTORICAL BUILDING
DES MOINES, IOWA

Volume XXII NOVEMBER 1961 Number 11

DISEASES *of the* Nervous System

A PRACTICAL JOURNAL ON PSYCHIATRY AND NEUROLOGY

Recent Developments in Psychoanalytic Research

ROBERT B. WHITE, M.D.

Currently there is great controversy as to which psychotherapeutic faith is the true belief. Indeed, there are those who question that psychotherapy of any sort is beneficial. After reviewing the literature on the effectiveness of psychotherapy, Eysenck (1952, 1961), a British psychologist, concluded that the available data failed to prove "that psychotherapy, Freudian or otherwise, facilitates the recovery of neurotic patients." Because Eysenck is an academic psychologist, we clinicians can easily dismiss his criticisms with the suggestion that he stick to running his rats through mazes and leave the treatment of patients to us. If we are psychoanalytically inclined, we can probably also ignore Raimy's (1950) description of psychotherapy as "an unidentified technique applied to unspecified problems with unpredictable outcomes. For this technique we recommend rigorous training."

Criticisms leveled specifically at psychoanalytic treatment are even more pointed and some are so telling that they cannot properly be ignored by even the most ardent Freudian. One critic states: "An analyst, let us say, of established prestige and seniority, produces a paper advancing some alleged discovery. . . . Given sufficient enthusiasm . . . or . . . just plain dogmatism on the part of the author, the chances are . . . this . . . alleged discovery will . . . be quoted . . . until it [becomes] an accepted conclusion [and] . . . is ultimately canonized with the sanctifying phrase 'as so and so has shown.' In other words an *ipse dixit* acquires the validity of an attested conclusion on hearsay evidence only." This critic is no academic psychologist like Eysenck; neither is he a skeptical neurosurgeon like Percival Bailey (1956), nor an unreconstructed organicist like Sargant (1961) who flail away at psychoanalysis at every opportunity. He is Edward Glover (1952), as orthodox a Freudian as ever sat beside a couch. Similar criticisms by another outstanding analyst, Lawrence Kubie (1949, 1961) have helped to stimulate many of the current systematic studies of psychoanalysis and psychotherapy by means of sound movies and independent observers.

Psychotherapy is not the only type of psychiatric treatment that has been called to account in recent years. Double-blind studies have questioned the effectiveness of a number of other treatment methods, including some of the psychotropic drugs which were described only a few years ago as "miracle drugs." For example, only a short time after Robie (1958) hailed Marsilid as the best news of the year for psychiatry, the study by Cole and Patterson (1959) concluded that "there is no difference in the efficacy of [Marsilid], of an inert placebo, or of psychotherapy in the treatment of depression as a symptom." Alexander's report (1958) that Deprol is an effective treatment for depression has been disputed by Bellak, et al. (1961). Insulin coma therapy and carbon dioxide narcosis have recently been investigated by carefully done double-blind studies. Ackner, et al. (1957), found that acute schizophrenics respond just as well to repeated comas induced by barbiturates as they do to comas from insulin. Hawkings and Tibbetts (1956) reported identical results in neurotic patients who inhaled or-

From Austen Riggs Center, Inc., Stockbridge, Massachusetts.

Presented at the second annual meeting of the Titus Harris Society, Beaumont, Texas, September 16, 1961. This paper results from a research program supported by grants from the Rockefeller Brothers Fund and the Ford Foundation.

dinary air from a pressure tank as in those who were narcotized by inhaling carbon dioxide.

My emphasis on these reports of skeptics is not because I am a therapeutic nihilist or an apologist for psychoanalysis. If anything, I err in the opposite direction on both issues. I mention them in order to stress the need for maintaining a constructively critical attitude toward all forms of psychiatric treatment—drugs, shock therapy, psychoanalysis, or whatever. For example, the recent emphasis on the placebo effect, better called, I believe, the hope-faith effect, challenges many of our assumptions about various forms of psychiatric therapy. The idea that hope and faith induced in the patient by the faith and hope that the doctor has in his particular method of treatment is, of course, not a new idea. However, the current trend of systematic investigation of the phenomenon is new.

Cotton's cure for schizophrenia which was the sensation of the meeting of the American Psychiatric Association in 1922 is a sobering example of the consequence of ignoring the power of the hope-faith effect. Cotton (1922) claimed that he could cure 80% of the schizophrenics in state hospitals through the elimination of foci of infections by radical surgical excision of teeth, tonsils, gall bladders, cervices, seminal vesicles, and, all else failing, the entire large colon. An independent evaluation by Greenacre (1948) showed that after five years there were fewer remissions and recoveries among the treated patients than among those who received only custodial care. She concluded that Cotton's enthusiastic research project had benefited patients by implanting an infectiously hopeful attitude in the staff rather than by removing foci of infection from patients. She commented: "Most impressive . . . was the influence of the therapeutic wish ambition, and enthusiasm of the director of the hospital on the majority of his staff who were devoted to and identified with him. The place hummed with pleasant inspiration."

A carefully done study by Feldman (1956) on the effect of Thorazine on chronic psychotics emphasizes the importance of the psychiatrist's enthusiasm or pessimism about a given method of treatment in determining how his patients will respond to it. Doctors who believed in the drug usually got good results; for example, one optimist obtained a significant improvement in 77% of his patients. Doctors who had no faith in the drug got poor results; for example, one pessimist obtained improvement in only 10% of his patients.

The increase in attention given to patients and the increased sense of hope among patients and staff that occur when a research project is begun on a ward may have a powerful therapeutic effect, as shown by Cotton's experience and by the more recent studies by Frank (1952), Rashkis and Smarr (1957), and others.

Curiously enough, it is an anesthetist, Beecher (1955, 1956, 1960, 1961), who has done some of the most outstanding work on the placebo, or hope-faith effect. In a remarkable double-blind study of the effectiveness of ligation of the internal mammary artery for the treatment of angina pectoris, Beecher (1961) found that whether the arteries were ligated, or whether the patient received only an anesthetic and skin incision, the results were identical both as to subjective improvement in symptoms and objective improvement in the electrocardiogram and exercise tolerance.

Among psychiatrists, Jerome Frank has been one of the most active investigators of the placebo effect. In his recent book (1961) he reviews a number of studies of this phenomenon, including his own project (Rosenthal and Frank, 1956; Gliedman, et al., 1958). He refers to a particularly hazardous-sounding experiment performed by Volgyesi (1954) on patients who were treated only with hypodermics of distilled water during hospitalization for bleeding peptic ulcer. Of those patients to whom a physician gave the injection with the assurance that it was a new, very effective medicine, 70% became symptom-free for over a year. Of those patients to whom a nurse gave the injection with the comment that

it was an experimental drug of unknown effectiveness, only 25% significantly improved. These and other papers on the placebo effect by Wolf and Pinsky (1954), Lasagna, et al. (1954), Shapiro (1959), and others, raise many challenging questions that are relevant to psychiatry and especially to psychotherapy.

We need not feel ashamed, as we sometimes tend to do, if research shows that the hope-faith effect is an important aspect of all psychiatric treatment. Karl Menninger has emphasized (1959) that a sense of hope is crucial in our work. Indeed, hope is essential for life itself; as Richter (1957) and Cannon (1957) have shown, without hope people and experimental animals die.

Psychoanalysts assume that their method of treatment involves a good deal more than inducing hope and faith in patients. In fact, psychoanalysis was developed out of dissatisfaction with hypnotic suggestion—a treatment based largely on the patient's faith. Until recently there have been no data available about the nature of the very complex process of psychoanalytic treatment except accounts given by the doctors who conducted the treatment, and they are admittedly partisan reporters. This state of affairs has caused Kubie (1961) to feel that a nonparticipant observer is mandatory for an objective study of any psychotherapy. Lack of data about the psychoanalytic process acceptable to nonanalysts has created much of the acrimony and confusion between proponents and opponents of psychoanalysis. Sternberg, Chapman, and Shakow (1958), a group sympathetic to psychoanalysis, comment: "In the absence of objective data, psychoanalytic concepts remain striking speculations not open to definitive study. It becomes meaningless to think in terms of . . . [a single] process [of therapy], since one therapist does not really know what the next one does except through partial and somewhat distorted reports, and the effects of the method cannot be determined." In considerable measure this lack should be remedied in the coming few years as the results of a number of new, well-organized research studies on psychoanalytic treatment become available. Noteworthy among these are the study by Leary and Gill (1959), the study by Shakow, Cohen, and others at NIMH, the work of Brody (1959), Scheflen (1961), English (1961), and colleagues, at Temple University on John Rosen's (1946, 1947, 1953) controversial technique of direct analysis of psychotics, and the very sophisticated psychotherapy research project of the Menninger Foundation conducted by Robbins, Wallerstein, Sargent, and others (1956, 1958, 1960).

Other studies directly or indirectly bear on the question of psychoanalytic theory, rather than on practical matters of therapy. Particularly relevant are the experimental studies on sensory deprivation, subliminal perception, and dream deprivation. As my colleague, Stuart C. Miller (in press), has shown in a comprehensive review of the literature, much of the recent work on sensory deprivation is of direct pertinence to psychoanalytic ego-psychology, especially to Rapaport's concept of the relative autonomy of the ego (1951, 1958). Among the outstanding reports on sensory deprivation are those of Azima and Cramer (1956), Bexton, Heron, and Scott (1954), Doane, Mahatoo, Heron, and Scott (1959), Goldberger and Holt (1958), Heron, Doane, and Scott (1956), Lilly (1956), Scott, Bexton, Heron, and Doane (1959), Shurley (1960). The reports of Klein (1959 a, 1959 b), Fisher and Paul (1959), and others, emphasize the importance of recent experiments on subliminal perception that bear out several basic psychoanalytic assumptions about unconscious mentation and dream formation. The work of Dement (1960) on dream deprivation supports the basic psychoanalytic proposition that dreaming plays an important part in maintaining our psychic equilibrium. Any discussion of work on psychoanalytic theory would, of course, be incomplete without mention of Rapaport's two recent comprehensive surveys of this field (1960 a, 1960 b).

Clinical research relevant to, but not directly about, psychoanalytic psychotherapy includes the work of Gill and Brenman (1959) on hypnosis, Erikson's (1950, 1958,

1961) delineation of the psychosocial stages of ego-development, the work of Burnham (1961) and his colleagues at Chestnut Lodge on the social-psychological aspects of hospitalization, and the studies at Riggs by Miller, Talbot, Polansky, and myself on the development of a therapeutic community in a psychoanalytic sanitarium (White, 1952 a, 1952 b, 1953, 1955; Polansky, et al., 1955, 1957; Talbot, et al., in press).

Of these various studies, I will discuss in detail the NIMH and the Menninger projects on the nature of psychoanalytic psychotherapy, the experiments on subliminal perception, the work at Riggs on the therapeutic community, and Dement's work on dream deprivation.

Psychotherapy Research Project of the Menninger Foundation

This is a study of 42 patients, half of whom have been treated by formal psychoanalysis and half by psychoanalytically oriented psychotherapy. The data used in the study are gathered at three different points: before treatment begins (designated the initial study), shortly after treatment ends (the termination study), and two years after treatment (the follow-up study). The initial study is based on the clinical information routinely gathered during the diagnostic evaluation of patients at the Menninger Foundation. These clinical data are derived from interviews with the patient, interviews with his family, and diagnostic psychological tests. This material is gathered by the clinical staff, not by the research team. Only after therapy is concluded does either the patient or the therapist know that the case is included in the research study. Thus, the research staff has no part in, or influence on, the treatment of patients. Neither therapist nor patient is burdened with the potentially distressing knowledge that the case will be subject to scrutiny by outsiders, and therapy can proceed undistorted by research observations. (In this regard the Menninger project differs from the NIMH and Temple studies, in which both patient and therapist know that the sessions are being observed or photographed.)

When therapy is concluded, the patient, his immediate family, his therapist, and his therapist's supervisor, are interviewed by the research team. In addition, the researchers review the clinical notes made by the therapist in the course of treatment, and readminister diagnostic psychological tests to the patient. These are the sources of data for the termination study. The follow-up study takes place two years after treatment ends and is based on interviews by the research staff with the patient and sometimes with his relatives, friends, and employers, and another administration of diagnostic psychological tests.

Before treatment begins, one group of research workers, using the data obtained from the regular procedures for clinically evaluating the patient, organizes those data into three categories:

1. *Patient Variables,* those factors in the patient's personality and type of illness that are postulated to be important for treatment and its outcome.

2. *Situational Variables,* factors and events in the patient's life situation that will have a significant influence on the course and outcome of the therapy.

3. *Treatment Variables,* specific therapeutic techniques and the personal attributes of the therapist that will influence the process and form the climate of the interactions between patient and therapist.

In outline form here are all of the points covered in each of these categories. In applying these categories to clinical data, the research staff uses a manual that carefully defines the meaning of each.

Patient Variables

I. Sex and age
II. Anxiety and symptoms
  1. Anxiety
  2. Symptoms
  3. Somatization
  4. Depression and guilt feelings
    a. Depression
    b. Conscious guilt
    c. Unconscious guilt
  5. Alloplasticity
III. Nature of conflicts
  1. Core neurotic problem
  2. Current life problem

IV. Ego factors (and defenses)
  1. Self-concept
  2. Patterning of defenses
  3. Anxiety tolerance
  4. Insight
  5. Externalization
  6. Ego strength

V. Capacities factors
  1. Intelligence
  2. Psychological-mindedness
  3. Constitutionally endowed aspects of ego strength
  4. Capacity for sublimations

VI. Motivational factors
  1. Honesty
  2. Fee
  3. Extent of desired change
  4. Secondary gain

VII. Relationship factors
  1. Quality of interpersonal relationships
  2. Transference paradigms

VIII. Reality factors
  1. Presence of "neurotic life circumstances"
  2. Adequacy of finances to the treatment requirements
  3. Attitudes of significant relatives
  4. Physical health

Situational Variables

I. Situational factors
  A. Background
    1. Cultural
    2. Religion, ethics and values
    3. Education
  B. Interpersonal Relationships
    1. Family relationships (parental)
    2. Family relationships (own family)
    3. Friends, coworkers, colleagues, etc.
  C. Marital-sexual
  D. Living situation
    1. Home arrangements
    2. Financial
    3. Responsibilities
  E. Occupation
    1. Stability
    2. Occupational demands
    3. Compensation
  F. Community and leisure time
    1. Recreation and avocation
    2. Group participation
    3. Civic and cultural activities
  G. Physical
    1. Appearance and physique
    2. Handicaps
    3. Somatic illness

II. Each of these situational factors is evaluated in respect to the following psycho-situational dimensions:
  A. Degree of relevance in the individual life
  B. Amount of stress
  C. Degree of support
  D. Degree in which the situation is a crucial conflict area
  E. Extent of opportunity for self-realization, growth, autonomy
  F. Congruence of the situation to needs, interests, capacities
  G. Degree of situational mutability

Treatment Variables

I. Formal elements of the treatment
  A. Treatment modality
    1. Variations determined by the nature of the patient's illness
    2. Variations determined by reality events
    3. Variations determined by the therapist
    4. Variations determined by the supervisor
  B. Treatment instructions, general and special
  C. Special external circumstances that affect the treatment course
  D. The basic techniques of the treatment
    1. Suggestion
    2. Abreaction
    3. Manipulation
    4. Clarification
    5. Interpretation
  E. Types of subject matter
    1. The patient's past life and memories
    2. Reconstructions and memories of the conflicts of infancy and childhood
    3. The patient's current life situation
    4. The events of the treatment hour
    5. Dream and fantasy material
    6. Style and form of the patient's expression
    7. Accompanying affect of the patient's expression
  F. The goals of the treatment
    1. The goals of the patient
    2. The goals of the therapist
    3. Changes in goals

II. The process of treatment
  A. Life of the patient during treatment
  B. Significant new history
  C. Course of treatment
    1. Major themes
    2. Major transference paradigms
    3. Changes in symptoms
    4. Changes in impulse-defense configurations
    5. Changes in manifest behavior patterns
    6. Structural changes in the ego

7. The acquisition of insight, and its relation to changes in attitudes towards the self, others, things, and the illness.
8. Style and form of communication

D. Termination of treatment

III. Variables in the therapist and the climate of the patient-therapist interaction

A. Qualities of the therapist

1. Skill and experience
2. Need for supervision and how he uses it
3. Personal style and attitudes
4. Countertransferences
5. Age and sex

B. Climate of the therapy

Having organized their data in this manner, the research group then makes a comprehensive formulation of the importance of the data from each category of this outline for the outcome of the case. They next make a set of clinical predictions about the following points:

1. *Treatment recommendations*
   (1) Counseling
   (2) Supportive psychotherapy
   (3) Expressive psychotherapy
   (4) Psychoanalysis
2. *Nature of problems to arise in therapy*
   (1) Transference issues that will occur
   (2) Resistances that will be encountered
   (3) External events that will influence therapy
3. *Prognosis*
   (1) Changes in symptoms
   (2) Changes in adaptive pattern
   (3) Acquisition of insight and its relation to changed attitudes to self, others, things, illness
4. *Over-all prognostic and predictive statement*
   (1) Global estimate of outcome
   (2) Health-sickness rating scale and predicted changes in that rating

At the time of the termination study still further predictions are made:

1. How will the patient fare between termination and the follow-up study two years later?
2. How will he deal with the major events that are expected to confront him after treatment terminates?

These clinical formulations and predictions, with the reasons for making them, are written in essay style. Finally, these clinical formulations and predictions are converted into a set of formalized predictions which are cast as questions to which a yes or no answer can be given. In addition, each formalized prediction is accompanied by a statement of what evidence will be considered necessary to support or refute it. In all, for each patient about 70 different variables are assessed, and about 60 specific predictions are made.

By formulating systematic and explicit predictions from the clinical data, by making explicit the assumptions on which each prediction is based, by stating exactly what evidence will be acceptable to refute or confirm each prediction, and by executing all three of these steps before treatment is even begun, the research design forestalls the greatest evil that besets clinical research, that of post hoc reasoning by which almost any outcome can be explained.

The attitude with which these researchers have approached their task is especially noteworthy. They are not attempting to prove that psychoanalytic treatment is better than other forms of treatment. They are attempting only to see if a group of experienced analysts using readily available clinical data can make valid predictions about the course and outcome of psychoanalytic treatment, and if these predictions, the incorrect as well as the correct, can clarify the complicated processes of psychotherapy. Having stated in advance both what their predictions are and how they were arrived at, the researchers are in a good position to retrace the steps in their reasoning. By retracing their steps they hope to learn as much from their incorrect predictions as from their correct ones. In summary they state, "the goal of this project . . . is the development of a consistent and comprehensive set of hypotheses about . . . psychotherapy which can subsequently be verified, refuted, or modified in detail." They hope thereby "to achieve a comprehensive set of propositions . . . that will allow the setting up of experiments and . . . of process and outcome studies that will systematically test these propositions" (Wallerstein and Robbins, 1960).

This project, begun in 1954, is still incomplete. To date the initial study has been completed on all 42 patients, the termination study on 21 patients, and the follow-up study on 11 patients. Although the final results and conclusions of the study will not be available for several years, here are some of the notable preliminary findings.

1. In the hands of experienced clinicians, clinical data can be used to make meaningful predictions about psychotherapy.

2. Clinical data can be organized so that quantitative as well as qualitative analyses of them are possible (an aspect of the total research design into which I have not gone because of limitations of space).

3. Patients are surprisingly willing to participate in intensive research interviews despite anxiety caused by such interviews.

4. If performed tactfully by skilled clinicians, intensive research interviews have not been harmful to patients.

5. The clarity with which patients can describe what it was in their treatment that helped them does not necessarily correlate with the degree of benefit the patient has obtained. For example, some very inarticulate patients, who were definitely benefited by therapy, could only make such comments as, "I don't know what it was that made me change. I don't even remember what we were talking about most of the time. But after a while I began to feel and act differently." Other patients who were much less benefited were able to speak in vivid detail about the events of treatment with what seemed to be a good grasp of the meaning of those events.

6. Some patients who were treated with supportive psychotherapy without achieving much, if any, insight, had considerable relief from symptoms, lessening of disordered patterns of behavior, and growth of personality, although they were often totally unable to describe how this improvement had taken place.

7. Both the patient and the therapist are more willing to discuss the treatment freely with the research team if they feel that it was successful. If they were disappointed with the outcome, their accounts of what occurred in treatment tend to be halting, disjointed, and full of glaring inconsistencies. In such circumstances both the patient and the therapist usually talk more about their disappointment and frustration with the results than about what actually happened within the treatment itself.

8. Such a research study is threatening to the therapist who treats the patient. He almost always feels his professional ability and his personal worth are being made vulnerable to criticism by the researchers.

N.I.M.H. Project

At the National Institute of Mental Health, Robert Cohen, David Shakow, and their associates have made sound movies of each of the 500 sessions of a psychoanalytic treatment of one patient, a treatment conducted by an experienced analyst who does not participate in the research at all except by offering himself, his patient, and his method of treatment as the object of study. This microscopic study of psychotherapy contrasts greatly with the more macroscopic approach of the Menninger project. This use of sound movies as a research tool was first suggested by Kubie (1947).

In a recent report on this project, Robert and Mabel Cohen (1961) state that so far only the first ten of the 500 hours of the total treatment have been reviewed and analyzed. The film for each of these ten hours was viewed about eight times in order to develop adequate concepts and methods by which to study the entire set of films. Somewhat facetiously they note that at the present pace the study would last for about 25 years longer.

This kind of research intrudes severely into the intimacy and privacy of the relation of patient and therapist, a problem that has been studied by Sternberg, Chapman, and Shakow (1958) and by Shakow (1960). Surprisingly enough, most patients feel little apprehension at having their privacy invaded by qualified professionals. Therapists, on the other hand, experience considerable apprehension, at least initially. Sternberg et al. report that after a first exposure to the camera a therapist stated: "When I got into the room, I didn't know [why] . . . but I had anxiety. I was shaking and I was more concerned about the camera picking it up than . . . with the patient." The therapist noted that his anxiety soon abated, but added: "The patient actually was much less anxious than I was." In all, the interactions between patient and therapist do not seem to be seriously altered, or disrupted, by sound movies.

Cohen and Cohen noted that this type of

research approach creates difficulties for the observers as well as for the observed: "Despite our knowledge that the results of our [own] psychotherapeutic endeavors are at best only encouraging . . . we are capable of feeling outraged at the bumbling efforts of our colleague who has been bold enough to expose himself to our scrutiny." Others engaged in similar work react in the same way, and the Cohens feel this might explain why the literature is so rich in provocative theoretical formulations, but poor in verbatim reports of treatment sessions. They conclude: "This situation makes it mandatory that the therapist in a study of this sort not be a member of the research group."

A few preliminary practical therapeutic suggestions have come from this study. Cohen and Cohen question whether "it really must take hundreds of hours to acquire the insights which are the basis or accompaniment of useful change," and whether "more effective use might not be made of the very considerable amount of information which is available in the early hours [of therapy]." They urge more experimentation in therapeutic technique, such as Renneker's (1960) suggestion that a recording machine be used regularly and that the patient or therapist be free to listen to sessions whenever either thinks it might be useful. The Cohens suggest experimenting with one session of therapy a week, tape recording each interview so that it could be intensively studied by the therapist and consultants in order to obtain the maximum amount of information before the next interview. "This procedure," they state, "might enable the therapist, within limits, to plan interventions in a more consistent and systematic fashion than is possible in the conventional analytic situation." In some instances, they suggest, the patient might be encouraged to listen to the recording by himself.

(This article will be concluded in the December, 1961, issue of *Diseases of the Nervous System*. The complete bibliography will be published at that time.)

Changes in Age Distribution of a Schizophrenic Population

G. DONALD NISWANDER, M.D., and GEORGE M. HASLERUD, PH.D.

Recently at the New Hampshire State Hospital a question was posed concerning aging in the chronic hospitalized schizophrenic population. This original query evolved from the attempt to predict what accommodations might be necessary in future years for patients at the hospital.

The literature contains a number of articles by the United States Public Health Service relating to patterns of retention, release and death in first admissions to state mental hospitals. Public Health Monograph 58 shows, however, that there is so much difference in the policies among the different states that it is difficult to arrive at even a general idea of what these patterns are.[1] The monograph does not apply to the problem of aging in schizophrenia that has arisen in New Hampshire. Kramer and Pollack, in approaching the problem in a different manner, depend upon a theoretical trend line from which they calculate the discrepancy between the prediction on the basis of past performances, and the actual reported number of individuals in the information supplied them.[2]

Data from the New Hampshire State Hospital may have special pertinence in answering problems concerning the chronic hospitalized schizophrenic patient. This hospital is the only facility for the mentally ill within the confines of the state. The hospital therefore provides treatment and care for all persons in the state except for those in private institutions and those entitled to hospitalization in a veterans' facility. New Hampshire also has a mature and stable population like

From the Arthur P. Noyes Institute for Neuropsychiatric Research, New Hampshire State Hospital, Concord, N. H.

that which the United States might anticipate in the next decade or so.

Since the opening of the hospital in 1842 some 41,000 patients have been cared for at the New Hampshire State Hospital. From those patients whose hospital records had been completed by reason of being discharged or having died, a 10 per cent representative sample was picked and relevant data was punched on machine-sorting cards for all cases up to the period of June 30, 1960; a 100 per cent sample of the present hospital population was likewise catalogued. From both of these samples, representative cross-sections were sorted out for 1930, 1940 and 1950. An individual who had died or had been released before 1960 would come into the various cross-sections from the 10 per cent sample. Those individuals in the hospital on June 30, 1960 whose stay overlapped any of the three cross-sections could be identified and followed, of course, with the 100 per cent sample adjusted to the 10 per cent sample. This present study thus empirically gives the actual outcome of continuance, release, or death in the representative sample in contrast to the statistical trend line of other studies.

One of the interesting findings of this study is that the differences between the male and female schizophrenic patients are so great that the data need to be presented separately.

Early in the tabulation of this data it was noted that there was a striking difference between the decades in the numbers of schizophrenic patients that had been hospitalized for ten years or longer. Based upon a rate per 1000 schizophrenic patients, this number had increased in the male schizophrenic patients from 426 in 1930 to 582 in 1950 and even further to 671 in 1960, the latter figure based on the 100 per cent sample. Similarly, the female schizophrenic patients in the hospital for more than 10 years increased from 514 per 1000 in 1930 to 711 in 1960, the latter based on the 100 per cent sample.

Figure 1 graphically gives the mean values for each complete decade of the ages of admission, discharge, and death of the 10 per cent sample of the male and female schizophrenic patients. Tables I and II give the comparable cross-sections on a special day, June 30th, at the beginning of each decade and the follow-up in the same period.

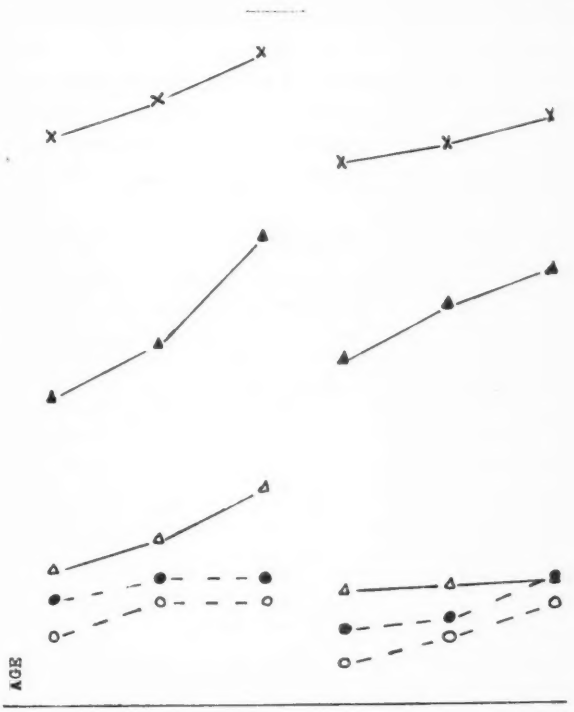

AGE
o——mean age at admission for those later released
●——mean age at release
Δ—— mean age at admission for those retained in hosp
▲—— mean age at death for those retained in hospital
X—— median age at death for New Hampshire normal pop

Fig. 1. Mean years of age between admission and release compared with mean years of age between admission and death for those retained in the hospital, the latter compared with median age of death in New Hampshire.

Another early observation was that the mean years of hospitalization of the schizophrenic patient dying in the hospital had changed tremendously from 1930-39 to 1950-59. In this group of patients the mean years of hospitalization for the females increased from 13 years to 19 years, and in the male population from 17 to 23 years, as can be seen in Figure 1. It is to be noted that during the same period the mean years of hospitalization of discharged schizophrenic patients did not change significantly. Both of these observations have significance for the questions with which this study began.

For both male and female schizophrenic patients who died in the hospital the mean age of death is far below the median age

of life expectancy of the normal New Hampshire population as can also be seen in Figure 1. This finding alone leads to many interesting speculations about physical illness and cause of death in the continuously hospitalized schizophrenic population.

TABLE I

Age distribution per 1000 female schizophrenic patients in a representative 10% sample at the New Hampshire State Hospital as of June 30th at the beginning of each decade, except 1960 where the sample is 100%. In parentheses are the hospitalizations continued to the end of the decade.

Age	1930	1940	1950	1960
65+	159 (32)	75 (32)	105 (72)	262
50–64	176 (145)	277 (234)	384 (303)	376
35–49	498 (367)	466 (339)	278 (230)	282
0–34	166 (132)	183 (119)	233 (103)	78

TABLE II

Age distribution per 1000 male schizophrenic patients in a representative 10% sample at the New Hampshire State Hospital as of June 30th of the beginning of each decade, except 1960 where the sample is 100%. In parentheses are the hospitalizations continued to the end of the decade.

Age	1930	1940	1950	1960
65+	55 (27)	95 (3)	114 (32)	150
50–64	171 (116)	219 (128)	251 (210)	454
35–49	449 (340)	467 (350)	495 (351)	285
0–34	323 (212)	219 (171)	139 (98)	112

Tables I and II show age distribution for both male and female schizophrenics in the hospital on June 30th in 1930, 1940, 1950, and 1960. One will note that within the forty years the schizophrenic population has shifted from a young to an old group. Note that there has been a decreasing number of patients less than 49 years of age in both sexes, whereas there has been a corresponding and significant increase in the number of patients in the age group of 50 years and over. In parentheses are shown the actual number of patients carried over from one decade to the next. The tables also locate the changes in age distribution for both sexes.

The value of this particular investigation is that it presents an empirical follow-up over 40 years of *particular* schizophrenic individuals in representative samples at the New Hampshire State Hospital. The shift in ages of the schizophrenic patients should be of special interest to the mental hospital administrator. One might surmise that in future years large mental hospitals will have a geriatric problem from the aging schizophrenic patient in addition to the usual geriatric patients admitted to the hospital from the normal community for the first time.

The relationship of this data to geriatric problems will be presented in another paper, as will also causes of the relatively earlier than normal death of hospitalized schizophrenic patients. An attempt will be made to predict the future schizophrenic population in a mental hospital.

Acknowledgment: The authors are indebted to Mr. John R. McLane, Jr., Chairman of the Board of Trustees of the New Hampshire State Hospital, whose original question stimulated the study; and further, to Edward Rutledge and Albert Anderson, Jr., for the statistical data.

REFERENCES

1. Patterns of Retention, Release, and Death of First Admissions to State Mental Hospitals. *Public Health Monograph No. 58*, 1959.
2. Kramer, M., and Pollack, E. S.: Problems in the Interpretation of Trends in the Population Movement of the Public Mental Hospitals. *Am. J. of Public Health*, 48:8, 1003-1019, 1958.

THE UNIVERSITY OF MICHIGAN MEDICAL CENTER

A postgraduate course in Clinical Neurology will be given at The University of Michigan Medical Center, Ann Arbor, on March 20 and 21, 1962, by Dr. Russell N. DeJong and staff of the Neurology Department. Program will be sent upon request to Department of Postgraduate Medicine, University Hospital, Ann Arbor, Michigan.

Spectrographic and Chromatographic Studies in Psychotics as Influenced by EST

THOMAS M. RUNGE, M.D., SIDNEY W. BOHLS, M.D., SAM A. HOERSTER, JR., M.D., and NAWASA THURMAN, M.T.

This work was instituted as a screening study to detect any biochemical difference which may exist between psychotic and normal individuals. While this seems probable, and a number of investigators have reported promising leads,[1-18] the problem remains speculative.

In planning this study it has been our aim to utilize broad testing methods which might display some gross difference in the pre-treatment as compared with the post-treatment patient, and once such a lead is detected, to follow it up with more definitive techniques. In discussing this plan with Dr. H. R. Henze, Professor of Chemistry at the University of Texas, he suggested that we first try infra-red spectroscopy.

Material and Methods

Infra-red Spectroscopy

Serum is more suitable for study than urine due to the technique necessary for infra-red analysis of water free material. The water content of serum is readily removed by lyophilization with a freeze-dryer. Serum in the dried state is mixed with 0.5% potassium bromide compound and a pellet of this material is formed with a vacuum pump and pellet making equipment. The pellet is placed in an infra-red spectrophotometer and the regions from 2 to 16 microns recorded. (Fig. 1). Modification of this technique utilizing dialization, desalting, the slurry technique, and separation of serum components by electrophoresis followed by elution of the alpha component were performed in an attempt to produce more definitive spectrograms.

Over 800 specimens were examined by this technique, in addition to psychotics and normals, a dozen mongoloids, a myasthenia gravis, and several systemic illnesses.

Paper Chromatography

Paper chromatograms for the determination of amino acids are carried out as follows: Urine is applied to Whatman #4 mm. chromatographic filter paper in microliter amounts with the concentration standardized for creatinine content. The amine acids are separated by two dimensional chromatography using phenol as the first solvent and 2,6 lutidine as the second solvent. They are stained with ninhydria, a dye for which amino acids have a specific affinity.

Chromatograms for indoles are prepared

From Austin State Hospital, Austin, Texas.

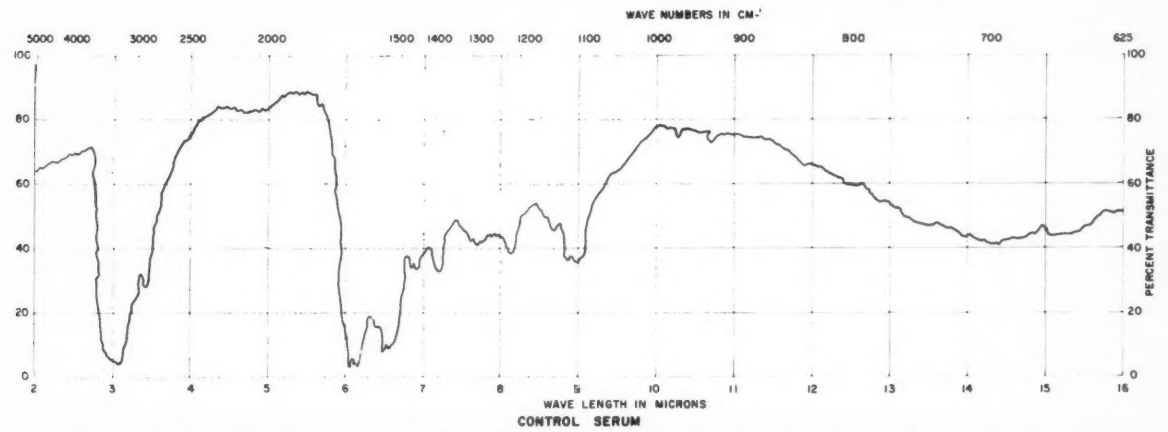


Fig. 1. Infrared spectogram over entire 2-16 micron region (control serum).

as follows: urine is applied to Whatman #3 mm. chromatographic filter paper in microliter amounts as above. Indoles are separated by two dimensional technique using isopropanol ammonia as the first solvent and butanol acetic acid as the second. They are stained with Ehrlich's reagent—paradimethylaminobenzaldehyde, each indole exhibiting a particular color and migration point.

To date we have performed over 200 chromatograms on urine specimens taken from patients before and after treatment and on controls.

Results

Infra-red Spectroscopy

The pattern shown in Figure 1 is that of a control and Figure 2 is that of a schizophrenic before treatment. The difference in the curve in the vicinity of 6-7 microns will be noted, the schizophrenic having a lower peak in this area as compared with the control. We were particularly intrigued with this finding since after treatment, some of the schizophrenics showed a more "normal" configuration as shown in Figure 3, which is that of the same patient as Figure 2, but after EST.

However in a series of 47 schizophrenics before and after EST this change was noted in only 32% after treatment. In a larger series of 84 schizophrenics studied only before treatment, the "low" curve was noted in 43% as compared with 20% of 20 controls. Our criteria for a "low" peak was one of 1.9 cm or less.

Another interesting finding was that the "psychotic" spectrogram could be simulated by incubating certain psychotomimetic drugs with normal serum. Figure 4. Three cc. of control serum plus 20 mg. mescaline. Adrenochrome produced similar results.

However, one psychotomimetic drug produced a different effect on the chromato-

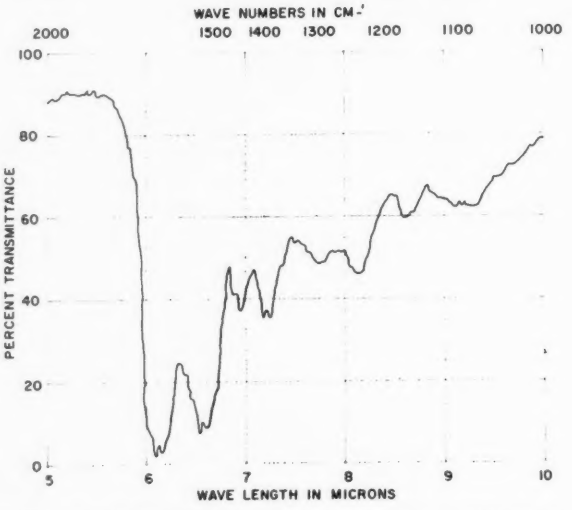


Fig. 3. Infrared spectogram of same patient as figure 2, but after EST.

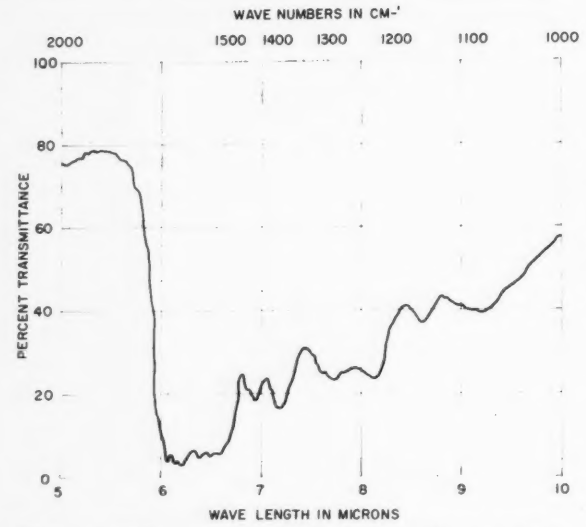


Fig. 2. Infrared spectogram of patient before treatment.

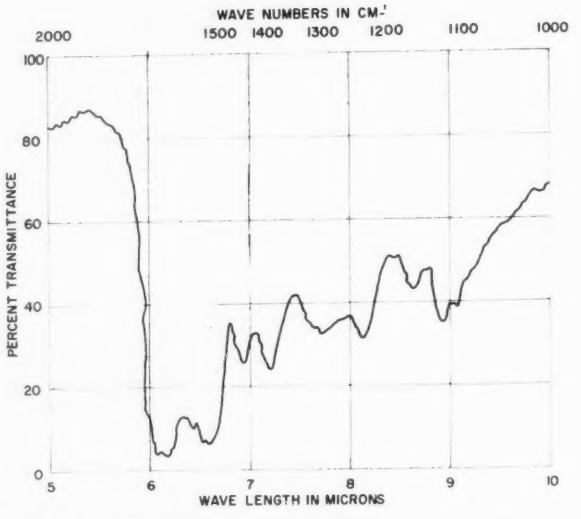


Fig. 4. Infrared spectogram of serum with 20 mg. mescaline added to 3 cc's of serum.

gram, namely bufotenine, which produced a taller peak in the 6-7 micron area.

In summary, our findings in infra-red spectroscopy of serum specimens included the detection of a pattern which is seen in most normals (16 of 20 controls), and which can be modified by incubation with psychotomimetic drugs. The most labile part of the spectrum is that from 6 to 7 or 7½ microns. Changes in this portion of the spectrum were noted in some psychotics after treatment, but not consistently so.

Because of the small number of cases and the absence of psychiatric confirmation of normalcy in the controls, it is not proposed that a "normal" infra-red spectrum has been established, and since the patients were uncontrolled from the standpoint of medication other than EST, the variations in the psychotic spectrum may represent artefact.

Chromatography

Amino Acid Chromatograms

A number of specimens have been examined by the method of amino acid chromatography. No consistent differences were noted in a small series of such chromatograms nor in several rabbit urine chromatograms before and after EST.

Subsequently work with the indole chromatogram has revealed an increase in tryptophane and its breakdown products in several patients after EST. This interesting finding has not been statistically significant is a small series so far studied.

Discussion

The possibility of a defect in tryptophane metabolism in schizophrenia has been raised by other investigators[19-22] and our study would suggest that there might be some such abnormality. Namely it appears that in some schizophrenics after EST there is an increase in urine tryptophane and its byproductcs as demonstrated by indole chromatograms. It is also interesting that in rabbits there is similarly an increase in tryptophane and its byproducts after administration of bufotenine and that apparently the psychotomimetic effect of this drug can be ablated in the rabbit through the administration of EST.

Since our series is small and not controlled as regards medications other than EST, we can draw no definite conclusions. Most of our patients received chlorpromazine or other phenothiazines and this group of drugs would almost certainly produce a significant effect upon this study, since animal work suggests that chlorpromazine antagonizes serotonin.[23-26]

One particular figure in our series is worth mentioning. In six schizophrenics who displayed no tryptophane in the amino acid chromatogram before EST, after EST tryptophane presented itself either directly or as an increase in indoles in five of the six patients. One might therefore surmise that EST literally knocked the serotonin (or more broadly the trytophane series) out of these patients.

Regarding the infra-red spectra, a number of interesting patterns have been obtained and their significance may be clarified by a more critically controlled series of patients now under study.

Summary

A technique has been demonstrated for the study of patients before and after EST by the method of infra-red spectroscopy and amino acid and indole chromatography utilizing sera and urine. Several interesting patterns have been obtained. Further work by this approach may be fruitful in better understanding the mode of action of EST and the metabolism of the central nervous system.

Acknowledgment is extended to Dr. Fred Lara who supervised the animal work.

BIBLIOGRAPHY

Biochemical Defect in Schizophrenia

1. Mann, P. J. G., and Quastel, J. H.: Benzedrine and Brain Metabolism. *Biochem. J.*, 34:414, March 1940.
2. Gottfried, S. P.: Serum Protein Fractionation Studies on Schizophrenia. *Psychosom. Med.*, 11: 334, 1949.
3. Holmberg, C. C., and Laurell, C. B.: Oxidase Reactions in Human Plasma Caused by Cerulo-

plasmin. *Scandinav. J. Clin. and Lab. Invest.*, 3:103, 1951.

4. Funkenstein, D. H., Greenblatt, M., and Solman, H. C.: Nor-epinephrine-like and Epinephrine-like Substances in Psychotic and Psychoneurotic Patients. *Am. J. of Psychiat.*, 108:652, March 1952.
5. Wooley, D. W., and Shaw, E.: A Biochemical and Pharmacological Suggestion About Certain Mental Disorders. *Science*, 119:587, April 30, 1954.
6. Martens, S., Leach, B. E., Heath, R. G., and Cohen, M.: Glutathione Levels in Mental and Physical Illness. *Arch. of Neurol. and Psychiat.*, 630, Dec. 1956.
7. Leach, B. E., Cohen, M., Heath, R. G., and Martens, S.: Studies of the Role Ceruloplasmin and Albumin in Adrenaline Oxidation. *Arch. of Neurol. and Psychiat.*, 635, Dec. 1956.
8. McGreer, P. L., McGreer, E. G., and Gibson, W. C.: Aromatic Exiretory Pattern of Schizophrenics. *Science*, 123:1029, June 8, 1956.
9. McFraw, P., and Boulding, J. E.: Relation of Aromatic Amino Acids to Excretory Pattern of Schizophrenia. *Science*, 123:1078, June 15, 1956.
10. Heath, R. G., Leach, B. E., Cohen, M., and Angels, C.: Effect of Behaviour of Humans with Administration of Taraxein. *Am. J. of Psychiat.*, 11(1):15, July 1957.
11. Angel, C., Leach, B. E., Martens, S., Cohen, M., and Heath, R. G.: Serum Oxidation Tests in Schizophrenia, and N,N-dimethyl-p-phenylenediamine Oxidation rates and Glutathione Concentration. *Arch. of Neurol. and Psychiat.*, 78 (5):500, Nov. 1957.
12. Fabisch, W.: Excretion of Hippuric Acid in Schizophrenia and Depressed Patients After EST. *Psychosom. Med.*, 19:320, July-Aug. 1957.
13. Frohman, C. E., Goodman, M., Luby, E. D., and Senf, R.: Ceruloplasmin, Transferrin, and Tryptophan in Schizophrenia. *Arch. Neurol. and Psychiat.*, 79:730, June 1958.
14. Bogoch, S.: Cerebrospinal Fluid Neuraminic Acid Deficiency in Schizophrenics. *Arch. of Neurol. and Psychiat.*, 80(2):221, August 1958.
15. Monaco, P.: Blood Amino Acid Levels During Insulin Coma in Man. *Archivio Di Fisiologia*, 58(1), 127, Apr. 15, 1958.
16. Busaino, G. A., and Stefanachi, L.: Urinary Excretion of 5-Hydroxyindolacetic Acid in Psychotic and Normal Patients. *Arch. Neurol. and Psychiat.*, 1:78, July 1958.
17. Frohman, C. E., and Luby, M. D.: Ceruloplasmin, Transferrin, and Tryptophan in Schizophrenia. *Arch. of Neurol. and Psychiat.*, 6:730, June 1958.
18. Atwood, R. P., and Green, J. P.: Comparison of Cerebrospinal Fluid from Schizophrenic and Non-Schizophrenic Patients on the Basis of Reactivity with Bial's Orcinol Reagent. *Fed. Proceedings*, 18(1):364, March 1959.

Tryptophan Defect in Schizophrenia

19. Cafruny, E. J., and Domino, E. F.: Urinary Excretion of Some Products of Tryptophan Metabolism in Schizophrenic Patients. *Arch. of Neurol. and Psychiat.*, 79(3):336, March 1958.
20. Frohman, C. E., Goodman, M., Luby, E. D., and Serf, R.: Ceruloplasmin, Transferrin, and Tryptophan in Schizophrenia. *Arch. Neurol. and Psychiat.*, 79:730, June 1958.
21. Price, J. M., Brown, P. R., and Peters, H. A.: Tryptophan Metabolism in Porphyria, Schizophrenia, and a Variety of Neurologic and Psychiatric Disease. *Neurology*, 9(7):456, July 1959.
22. Brown, F. C., White, J. B., and Kennedy, J. K.: Urinary Excretion of Tryptophan Metabolites by Schizophrenic Individuals. *Am. J. of Psychiat.*, 117:63, July 1960.

Chlorpromazine Antagonism to Serotonin in Animals

23. Gyermek, L.: Chlorpromazine: A Serotonin Antagonist. *Lancet*, 2:724, 1955.
24. Benditt, E. P., and Rowley, D. A.: Antagonism of 5-Hydroxytryptamine by Chlorpromazine. *Science*, 123:24, Jan. 6, 1956.
25. Pennes, Harry H.: "Psychopharmacology, Pharmacologic Effects on Behaviour." New York, *Hoeber-Harper Book*, 1958.
26. Sobotka, H., and Stewart, C. P.: "Advances in Clinical Chemistry," Vol. 1, pages 194-224. *Academic Press, Inc.*, New York, 1958.

18 Medical Arts Square, Austin, Texas.

UNIVERSITY OF MINNESOTA

Medical continuation courses in Pediatric Neurology will be presented at the Center of Continuation Study, University of Minnesota, on February 12 to 14, 1962. For further information, write to the Director, Department of Continuation Medical Education, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14, Minnesota.

Two New Butyrophenone Derivatives Studied with the Conditioned Reflex Technique

G. F. GOLWURM, M.D., and F. VANNI, M.D.

Two new psychotropic drugs (R-1625 [4'-Fluoro - 4 (4'-4"-chloro phenyl)-4'-hydroxy-piperidine-butyrophenone] and R-1647 [4'-methoxy-4-1-(4'-phenyl)-1, 2, 3, 4-tetrahydro-pyridine-butyrophenone]) have been developed recently that are of considerable interest, since they are not derivatives of the phenothiazines but belong to the butyrophenone group.[1] The former is available in Europe under the name of haloperidol,[2] while the latter is still under investigation.[3]

We have used both experimentally in order to study their effects on psychic function. The conditioned reflex was examined and direct observations of behavior made during the experimental procedure, since these were considered the best methods for obtaining objective and measurable information on their neurodynamic action.

Material and Method

Four Albino male Sprague Dawley rats, weighing about 250 grams each, were used at each dosage level (44 conditioned and 16 partially conditioned rats were used in all). They had previously been conditioned to avoid a weak electric shock (U.S.) after the ringing of a bell (C.S.) for three seconds. Behavior was observed during 60 second intervals between two consecutive conditioned stimuli. The experiments lasted one hour a day, during which time the animals received 60 conditioned stimuli.

For the conditioning procedure we employed a Gellhorn cage,[4] and a cage with superimposed grate united by a column provided with an automatic cyclic commutator.[5] The latter makes the whole operation fully automatic and eliminates any subjective factors on the part of the investigator. The drugs were studied in animals in whom the avoidance response had been stabilized and constant for a period of time (the rats were considered well conditioned after they had been given about the same percentage of C.R. for one week), and in animals on the fourth day of learning. The latter had been trained only in the Gellhorn cage according to the method of Jacobsen.[6] The animal received 60 stimuli at 60 second intervals every day, and the experiments lasted four days. No drugs were administered during the first two days; on the third day a placebo was given, and on the fourth day the test substance was used.

We made a daily evaluation of the number of conditioned reflexes carried out, as well as the "emotional tension" according to the degrees proposed by Jacobsen. The substances were administered subcutaneously two hours before the experiment, both in the well conditioned animals and those in the phase of learning. Four rats at each dosage level were used.

Results

R-1625 (Table I) shows a remarkable deconditioning activity even at very low doses. Its action becomes evident at 0.025 mg./kg. and is very clear at 0.05 mg./kg. The dosage level at which this activity appears is fairly sharp. The unconditioned reflex disappears in an equally sharp manner although movement is still possible. The symptoms of catalepsy appear at higher doses and some difficulty in movement was also observed.

TABLE I

R-1625

mg/kg	Before treatment		2 hours after treatment		24 hours after treatment	
	CR	UR	CR	UR	CR	UR
0.01	62	+	74	+	90	+
0.025	82	+	46	+	66	+
0.05	79	+	0	±	78	+
0.10	88	+	0	—	25	+
0.50	88	+	0	—	56	+
1.00	80	+	0	—	76	+

From the Istituto di Clinica Psichiatrica Dell'Universita' Degli Studi di Milano. (Prof. C. L. Cazzullo.)

R-1647 (Table II) shows the first signs of deconditioning activity at doses 40 times greater than the preceding compound. The unconditioned reflex is never completely lost with the dose levels used. However, the relationship of dosage to activity on the unconditioned reflex and conditioned reflex is high. Once there is a 50% reduction in the C.R. at a particular dose level, it is necessary to use twice the amount of drug to obtain the same result with the U.R. Both substances in these studies did not show any activity beyond 24 hours.

TABLE II

R-1647

mg/kg	Before treatment		2 hours after treatment		24 hours after treatment	
	CR	UR	CR	UR	CR	UR
0.50	90	+	95	+	88	+
2.50	64	+	52	+	58	+
5.00	76	+	53	+	67	+
10.0	79	+	39	+	79	+
20.0	74	+	10	±	68	+

The data summarized in Tables III and IV are of interest. Spontaneous motility is the first to be influenced by both compounds. For R-1625 its decrease is proportional to the loss of C.R.; for R-1647 it diminishes before.

Experimental catalepsy produced with high doses of R-1625 is never present with R-1647. Ptosis, evident already with the smallest dose of R-1647, is noted with R-1625 only when catalepsy begins to appear.

The deconditioning action on rats in the learning phase and the evaluation of the "emotional tension" in situations of experimental conflict were studied. A series of experiments were carried out in a group of animals which were conditioned for four days only. The doses used in these experiments had little or no deconditioning activity in the well conditioned animal. We now found, however, that it was possible to inhibit the C.R. of animals at the learning stage before the recently learned C.R. was firmly established. For R-1625 the loss of the conditioned response is nearly total (Figures 1 and 2).

TABLE III

R-1625—Two Hours After Treatment

mg./kg.	CR	UR	Spontaneous motility	Catalepsy	Ptosis
0.01	+	+	+	—	—
0.025	±	+	±	—	—
0.05	—	±	—	—	—
0.10	—	—	—	—	—
0.25	—	—	—	±	±
0.50	—	—	—	++	+
1.00	—	—	—	+++	+
5.00	—	—	—	+++	++

TABLE IV

R-1647—Two Hours After Treatment

mg./kg.	CR	UR	Spontaneous motility	Catalepsy	Ptosis
0.50	+	+	+	—	—
2.50	+	+	+	—	±
5.0	+	+	±	—	+
10.0	±	+	—	—	+
15.0	—	—	—	—	++
20.0	—	±	—	—	++
25.0	—	—	—	—	++

R-1647 at dosage levels of 2.5 mg./kg., and 5 mg./kg. produced a very slight reduction in C.R. It was found that the U.R. affected the rat while moving in the cage. Either the animal did not cover the whole distance within the required time (three seconds after the bell finished ringing) or was uncertain and hesitant at the door between both.

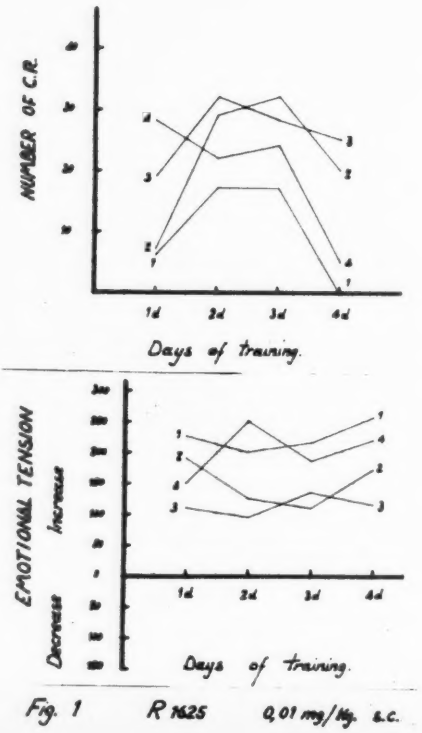


Fig. 1 R 1625 0.01 mg/kg. s.c.

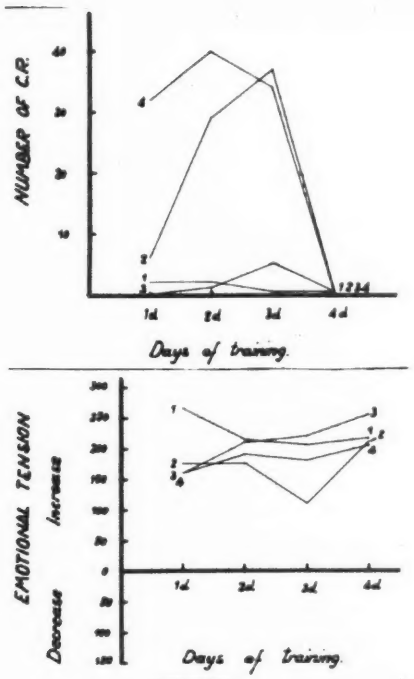


Fig. 2 R 1625 0,025 mg/kg s.c.

For R-1647 (Figures 3 and 4) there is a deflection which is often due to a delay in the response rather than to a real loss of the conditioned reflex activity. This deflection is parallel to a more marked deflection of the index of "emotional tension." On the other hand, with R-1625, symptoms of "emotional tension" increased, often with paroxysmal activity; spontaneous motility diminished. Both drugs reduced spontaneous movements as well.

Discussion

These preliminary data allow certain deductions regarding the activity of both compounds. Although their chemical structure is similar, they show different biological activity. In the case of R-1625, its activity is similar in many ways to the phenothiazines, even though it differs in other ways. The ability to inhibit the conditioned reflex is the first pharmacologic action which appears (inhibition of spontaneous motility). This activity is high, abolishing the recently learned C.R., and finally the U.R. In comparison to other substances (chlorpromazine and reserpine[7]) which are capable of deconditioning, it shows no activity in conflict situations, as expressed by the "emotional tension" in "electrized rats" (a term introduced by Boissier[7] indicating conflict-induced behavior in rats produced by the electric U.S.)

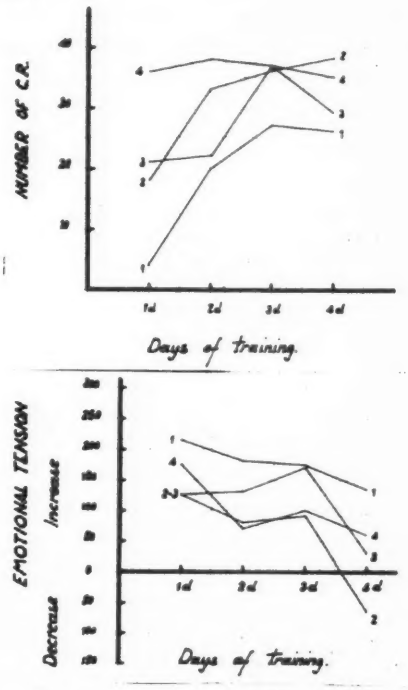


Fig. 3 R 1647 2^5 mg/kg s.c.

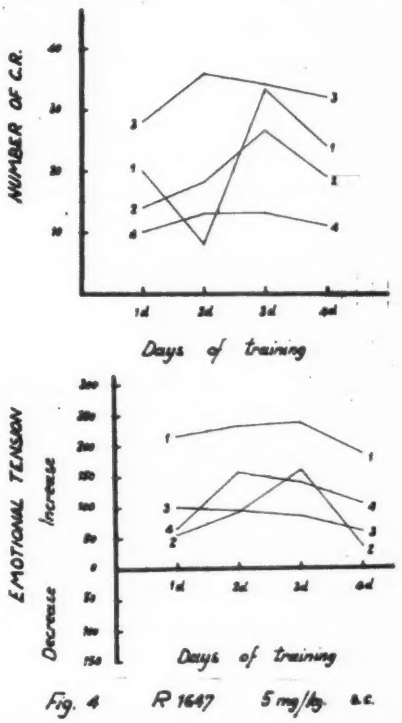


Fig. 4 R 1647 5 mg/kg s.c.

R-1647, on the other hand, showed little effect in abolishing the C.R., but diminished the "emotional tension" in experimental conflict situations. Contrary to R-1625, even at high doses, it does not produce catalepsy. Much before acting on the C.R. (at doses inferior to one-half the E.D.), it already shows pharmacologic activity on spontaneous motility in the rat and on palpebral ptosis. Nevertheless, it cannot be considered among the neuroleptics. It is equally difficult to place it in the group of the so-called anti-anxiety compounds (benactyzine, meprobamate) which have a high order of activity in conflict situations, although they, themselves, show no deconditioning activity.[8-10]

R-1625 acts electively on the association processes. It probably influences those associative memories acquired recently, and would favor the process of "cortical inhibition," if one considers the problem in a Pavlovian frame of reference. This cortical inhibitory action favors extinction of the conditioned reflex activity and "sub-cortical excitement" by a mechanism of "mutual induction," thus, being responsible for the symptoms of "emotional tension."

R-1625 favors inhibition in the same way as chlorpromazine. In the second series of experiments, besides the reduction of the C.R. and spontaneous motility, there was often an accentuation of disordered and incoordinated reactions, as well as excitement from stimuli of a painful nature with increased tension. This type of response seems connected to the infracortical centers which are free of cortical control. In Pavlovian physiology, this can be explained as a phenomena of positive corticosubcortical reciprocal induction.

At appropriate doses, R-1625 would seem to be indicated in those states where ideational disorders either are primary or play a predominant role. The resemblance to the biological activity of phenothiazines and reserpine leads us to believe that this compound would be active on the same psychotic symptoms as the former. It is inactive in neurotic states. Its ineffectiveness in conflict situations would confirm this supposition.

A final interesting consideration with R-1625 is the following: The effective dose at which it is active on the processes of higher psychic integration is much different from that required to produce catalepsy. This dissociation leads us to believe that a compound's therapeutic activity in man is not necessarily linked to its ability to produce an akinetohyperkinetic syndrome.

R-1647 at medium doses does not seem to influence associative processes; on the contrary, it appears to act on the emotional components of conflict. However, it cannot be considered in the group of anti-anxiety substances. It occupies an intermediate position, and its eventual role in emotional disorders remains to be evaluated experimentally.

Summary

1 .The influence of two new butyrophenone derivatives on the avoidance response and behavior in conflict situations of the rat has been studied.

2. A remarkable difference has been found in the activity of these two substances.

Acknowledgment: The authors wish to thank the Istituto Luso Farmaco d'Italia who provided the compounds used in this study.

BIBLIOGRAPHY

1. Janssen, P. A. J., van de Westeringh, C., Jagenau, A. H. M., Demoen, P. A. J., Hermans, B. K. F., van Dale, G. H. P., Schellekens, K. H. L., Van der Eychen, C. A. M., and Niemegeers, C. J. E.: Chemistry and Pharmacology of CNS Depressants Related to 4-(4-hydroxy-4 phenylpiperidino) butyrophenone. Part 1—Synthesis and Screening Data in Mice. *J. Med. Pharm. Chem.*, 1:281-297, 1959.
2. Cardani, A., Goldwurm, G. F.: Esperienze cliniche con un nuovo farmaco psicolettico (R-1625). *Riv. Sperim. di Freniatria,* 1960, in press.
3. Divry, P., Bobon, J., Collard, J., Pinchard, A., and Nols, E.: Expérimentation psychopharmacologique d'un nouveau neuroleptique: le R-1647. *Acta Neurologica Psychiatr. Belgica,* 9:1033-1044, 1959.
4. Munn, N. L.: "Handbook of Psychological Research on the Rat." New York, 1950.
5. Genovese, E., and Goldwurm, G. F.: Effetto di

differenti sostanze sullo scondizionamento esercitato dalla reserpina. *Atti del la Soc. Lomb. Scienze Medico Biologiche,* XIV:291-295, 1959.
6. Jacobsen, E., and Sonne, E.: The Effect of Benactyzine on the Conditioned Responses in the Rat. *Acta Pharmacol. Toxicol.,* 12:310-320, 1956.
7. Boissier, J. R.: Methodes d'études pharmacologique des substances dites tranquillisantes. *Thérapie,* XIII:1074-1118, 1958.
8. Holten, C., and Sonne, E.: Action of a Series of Benactyzine Derivatives and Other Compounds on Stress-Induced Behavior in the Rat. *Acta Pharmacol. Toxicol.,* 11:148-155, 1955.
9. Gatti, G. L.: Azione dei farmaci tranquillanti sui vari tipi di comportamento del ratto condizionato. In: "Psychotropic Drugs," (Ed.: Garattini, S., and Ghetti, V.), Amsterdam, *Elsevier,* 1957.
10. Jacobsen, E., and Sonne, E.: The Effect of Benzylic Acid Diethylaminoethyl Ester HCL (Benactyzine) on Stress-Induced behavior in the Rat. *Acta Pharmacol. Toxicol.,* 11:135-147, 1955.

Anorexia Nervosa:

Treatment with Hypnosis and ECT

HARRY K. DAVIS, M.D.

The disease entity of anorexia nervosa was first described by Lasaque when he called it "Historical Anorexia" in 1873. Sir William Gull in 1874[1] and 1888[2] again described the condition and called it "anorexia nervosa." Since this original description less than a hundred years ago, there have been approximately a hundred articles published in English regarding this subject.[3] The articles emphasize the rarity of the condition, as well as the poor therapeutic results obtained.

This case of anorexia nervosa is presented in detail since it did occur in a 12-year old, and because hypnosis was used as a diagnostic and therapeutic tool. Hypnosis was used to obtain an adequate history and to remove the distressing symptoms of anorexia, inability to walk and aphonia. The child communicated poorly and trance states were used to enhance the communication. Using only hypnotherapy, good nutrition and locomotion were rapidly re-established. This approach provided a more rapid removal of the disturbing symptoms and thus shortened the period of rehabilitation. Electroconvulsive therapy was used to treat the depression associated with this illness.

Case Presentation

C.H., a 12-year-old white female from a small Texas community was admitted to the University hospital on April 20, 1960. Little history was available at the time of admission even though she was accompanied by both the mother and father. The complete history was obtained by repeated interviews under hypnosis.

The patient was supposedly well until the fall of 1959. Prior to this time the patient had been a shy, seclusive, fearful and withdrawn child and had become increasingly so for the past three years. When school began in September 1959, the child was promoted from elementary to junior high school —a different environment and a different route to walk to school each day. In her shy and retiring state new friends and acquaintances were difficult to make. Her family is from a very low socio-economic stratum and other children teased her—told her she was ragged, dirty, no-good, and that her father was an alcoholic (a fact). These incidents continued and caused more withdrawal. The mother, working to provide a livelihood for the family, was too occupied to listen to her daughter's plea for help. Her brothers and sisters laughed at her when she told them how she feared and resented the children at school. She had a fourteen-year-old dog that she could talk to and felt he was the only friend she had. No one else would listen to her problems. The old dog died of a heart attack (she was told) and this upset her very much. In fact, the first amytal interviews consisted of loud outbursts of crying as she described each movement of her dying dog and ruminated over the fact no one tried to save the dog. A few days following the death of her dog in late September she became very disturbed and cried for three days. Late one evening as the child was going swimming, she was attacked by a local bully who had been teasing her. The boy threw her down, ripped her clothes and attempted to have coitus with her. As she tried to get away after the attack, the boy threatened to kill her if she ever told anyone about this incident.

About October 10th the patient became physically ill with a high fever and tonsillitis. Her doc-

From the Department of Neuropsychiatry, The University of Texas Medical Branch, Galveston, Texas.

tor treated the acute illness successfully but afterward the patient could not talk above a whisper. She became more depressed, cried frequently and refused to eat. The acute illness caused her to become weaker, and she was unable to attend school. She now walked with a limp, complaining she could not walk on her right leg without severe pain in the knee. (This knee had previously been bruised in a fall on the way to school when a boy was chasing her.)

Several attempts and methods were utilized to get the patient to walk, talk, and eat. She continued to refuse to eat and in November was hospitalized and given I.V. fluids. After hospitalization she improved. Eventually psychiatric care was sought locally, after which she was sent to this hospital. Her weight had fallen from 88 pounds to 58 pounds and she was too weak to get out of bed. She had threatened to kill herself on several occasions but had made no overt attempts. During her hospitalization she would say: "I want to die and I want to starve," "Let me alone—no one cares now and no one understands—Skipper (her dog) is gone and no one else cares."

During the last weeks prior to admission she dreamed practically every night of wild animals chasing her. These dreams terminated with the patient awakening in a panic state.

Past Medical History: Usual childhood diseases—no operations or significant injuries.

Personal History: C.H. was born in a small community and grew up there. The father was a laborer in a cotton compress plant and the mother a housewife. The patient's birth and early development were normal. She began school at the age of six years and did well for the next three years. She had always been retiring and shy but became much more so in the past three years. It was during this period that her father began drinking heavily, coming home drunk almost every night. He was loud and boisterous and frequently would physically and verbally abuse the mother and older children. No history could be elicited of any incestuous advances being made by the father, either intoxicated or sober. Patient's siblings are 23, 22, 21, 18, 15, 11, and 9 years of age. She had been a good student in school achieving A's and B's, doing higher scholastically than other members of her family. The family is Baptist but the patient was the only one who attended church regularly. Before her illness she had had hobbies of cooking, sewing, drawing, and reading. Patient denied having any previous sexual experiences and had received no education about menses or reproduction from parents.

Mental Status: This is a very shy, withdrawn, pale, dirty, ill-kept and anemic-looking child who is stooped and appears to be grossly fearful. She will not talk above a whisper, and there is no spontaneity in her talk or actions. She sits alone and looks away into the corner and does not make any effort to socialize or speak. Her psychomotor activity is markedly retarded. Her affect is somewhat flattened and shallow but is appropriate. She makes this mood statement: "I want to die—let me die." There is no history of hallucinations, delusions or illusions. The sensorium is clear; she is well oriented as to time, place, and person. Her memory for both past and present events is excellent. The retention and recall seem to be within normal limits for a child of this age. Judgment is somewhat impaired; however, she does have some insight into her illness.

Laboratory Studies were completely within normal limits.

Consultations: Because of the multiplicity of somatic complaints, she was seen in consultation with the departments of otolaryngology, orthopedic surgery, endocrinology, and psychology. The conclusion reached by the otolaryngology department was that there was no pathology found in the nasopharynx to cause the aphonia. The orthopedist's impression was that there was no pathology in the right knee found to keep this child from walking. A thorough workup by the endocrinologist ruled out hypopituitarism, Simmonds' disease, etc., and was in agreement with the diagnosis of anorexia nervosa. The conclusion of the psychologist was that this girl showed a hysterical neurosis with a full scale I.Q. of 98. However, it was thought the I.Q. test results were impaired because of the child's illness.

Hospital Course and Treatment: On admission April 20, 1960, nutrition was maintained by intravenous fluids and spoon feedings. An effort was made by the nursing service to care for this child's every need, and, in view of this, a student nurse was assigned to her on a full-time basis. During the next ten days an initial psychiatric interview, two amytal interviews, and a thorough physical evaluation were accomplished. These amytal interviews revealed much conflictual material but were abandoned because of the child's intense fear of the injections. Hypnotic trances were begun on May 2, 1960, and continued at regular daily intervals. These were usually of one hour duration. Her weight on May 2 was 61¼ pounds. With each hypnotic trance the patient was given the post-hypnotic suggestion that she eat and that food tastes good and that she needs it to live. She always replied under hypnosis that she wanted to die, she was not going to eat and that she did not like the taste of food. During the next few days she began to eat and did improve. By May 10 her weight was up to 65 pounds. From May 10 to 15 much conflictual material in the history was obtained plus much more depressive ideation.

By May 16 deeper trance states were induced, and I attempted to make the child walk under hypnosis. As the suggestion to walk was made, i.e.: "Stand up and take one step forward," she began to cry and show signs of fear. She described this fear as

seeing a vision (more like a spirit, ghost, and people combined). As the suggestion was withdrawn, the vision left. Before the trance was over, she envisioned a cat killed by a car. Under hypnosis on May 17 an attempt to produce anesthesia in the right leg was unsuccessful. With the suggestion that she stand up and take one step forward, she envisioned a green-headed monster with one bloody eye in the center of his head. The patient showed signs of extreme fright as she described the vision of the monster killing her mother and burying her. She now weighed 66½ pounds. On May 18 two trances were induced and the trance material discussed on a conscious level. The post-hypnotic suggestion was given for the patient to stand up and walk when awakening from the trance. She walked and continued to do so without difficulty. On May 20 attempts under a trance to remove the aphonia were unsuccessful. Her weight now was 70½ pounds.

In 18 days and 17 trances consisting of approximately 12 trance hours, the patient gained from 61 to 70½ pounds. She was cooperative and at times more contented. Practically every night she experienced terrifying nightmares of animals chasing her. Her weight gain is graphically illustrated in Figure 1.

Because of this girl's severe and profound affective disturbance of a depressive nature, it was felt that she should receive electroconvulsive therapy. On May 23, 1960, she received her first ECT. Treatments were also given on May 25, 27, 31, and June 2, 4, 7, 9, 13, 15, 17, and 20 to make a total of twelve ECT's over a period of approximately one month.

After electroconvulsive therapy was begun, the next four trances were introduced with ease. During the fifth trance after ECT's were initiated, she related in detail how she was sexually assaulted by a neighbor boy. Subsequent trances up to June 10 revealed more details of the sex act plus more depressive ideation. Her last ECT was given on June 20, 1960. I was unable to induce another trance state until July 6. She was dismissed to the home of her foster parents on July 16, 1960.

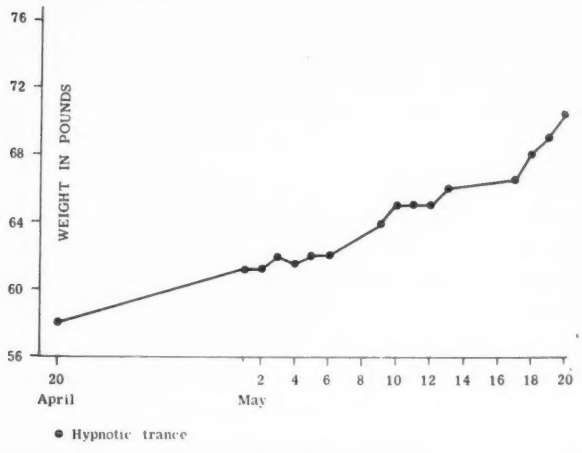


Figure 1.

Figure 2 demonstrates how electroconvulsive therapy affected the induction of the hypnotic trances.

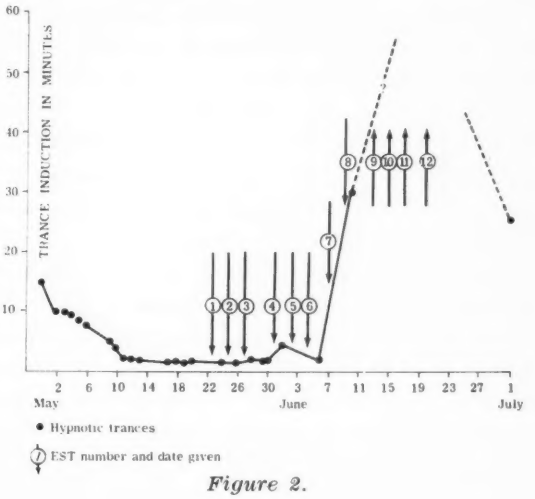


Figure 2.

Discussion

As is well known, anorexia nervosa is a rare disease entity. Several authors[3,4,6,8] found 1.2 to 1.8 admissions each year in very large hospitals. Cobb[7] found an incidence of 0.15% among general admissions in 153,934 admissions at Massachusetts General Hospital.

Our present day concept of the clinical syndrome is in general agreement with most authors.[3,4,8,9,10] At times the differential diagnosis may be difficult as anorexia nervosa is often confused with Simmond's disease. A thorough evaluation, especially of the psychiatric component, makes differentiation easy. Cole[12] lists a schematic formulation to differentiate the two diseases.

This disease characteristically occurs in young females. Our case of a 12-year-old girl is extremely unusual and as far as the author can find, there is only one other case reported where the patient is younger—a nine-year old. Two other cases occurring at 12 years of age have been reported by Gianakon.[13]

Several authors[4,5,8,10,13-16] in the cases reported, show the average age of onset of the disease to be approximately 18 years. As one peruses the literature, it is apparent that most any psychiatric disturbance in severe

form may cause the syndrome of anorexia nervosa. Most authors[3-5,8,9,13,14,17] agree that a certain basic personality structure is necessary as the basis of the psychopathology. This personality is regarded as perfectionistic, compulsive, excessively orderly, overly sensitive, immature or masochistic with lack of spontaneity. In addition to the basic personality, certain environmental stresses are necessary to produce the clinical syndrome.

Theories, involving the psychodynamics of the disease, have been advanced.[4,9,13,17-19] The psychodynamics of this patient incorporate several aspects of these various theories. Her rejection of all food as well as her refusal to communicate and locomote provided more attention for her. This rejection and withdrawal would prevent adult body development and would further her desire to die by starvation. She had no education about sex physiology, and there was no evidence to suggest that she had fantasies of oral insemination. Her basic personality make-up was the type characteristically seen with this disease. The symptoms had the function of expressing hostility toward her family. This was emphasized by her lack of desire to return home after treatment was terminated. In many respects this child showed psychological infantilism where food and feeding are a part of the relationship the child has with persons who care for her.

Anorexia nervosa is classified as a psychophysiological gastrointestinal reaction by the American Psychiatric Association nomenclature, Noyes and Kolb,[11] and Smith.[20] Kay and Leigh[8] believed three-fourths of the cases were hysterical and the remaining one-fourth were schizophrenic or depressive, while Yaskin and Brill[11] entertained a diagnosis of schizophrenia or depression.

The author was able to find only one other case of anorexia nervosa reported in the English literature that had been managed either totally or partially by hypnosis and hypnotherapy. This was a case reported by Birnie[16] in 1936. He reported a case of a 16 year old girl with vomiting and anorexia occurring with a grief reaction. This followed a girl friend's move to another locale and her subsequent death from burns. The symptoms were accentuated by a very domineering mother who forced the patient to eat. In our present day considerations this case seemed an early case with mild symptomatology. The patient was hypnotized weekly for a total of 14 times over a period of three months. With this treatment she returned to her usual weight. Post-hypnotic suggestion was used to encourage her to eat the foods she liked.

As aforementioned, the results in the treatment of anorexia nervosa have been universally poor, and are definitely related to the underlying psychopathology. Psychotherapy, superficial[10] and intensive,[14,19,22,23,25] environmental manipulation with environmental support,[4-8] electroconvulsive therapy,[8,14,24,26] lobotomies,[9] subshock insulin,[26] reserpine,[4] hypnosis,[16] and tranquilizers[15] have been used. Selection of the type therapy should depend entirely on the psychiatric illness and type therapy available.

Nemiah[3] reviewed 15 large series and showed a total of 282 patients with recovery in 128 (45.7%), 69 (24.5%) improved, 62 (21.9%) chronically ill, and 22 (7.8%) died.

According to Kay, 1953,[25] regardless of the type of therapy used, only slightly more than half are improved and 15 per cent die. The majority of the improved ones are neurotic personalities and only 10-20 per cent recover with a good adjustment.

Recently West[27] postulated that hypnosis is mediated through the ascending reticular system. Figure 2 illustrates how ECT interfered with the hypnotic trance. This prolongation and eventual inhibition of trance may be due to the effect of ECT on the reticular system.

The results of the case reported seem good. Even though five months have elapsed since leaving the hospital, the patient continues to do well. Her weight remains constant, she is doing well in school, and is relating well to her foster parents. Since returning home she is learning to play the piano and drive a car. No depressive ideation has returned, and the aphonia that was

persistent throughout her illness is gradually disappearing.

Summary

A review of the literature is presented along with a most unusual case occurring in a 12-year old female. Hypnosis was used as a method to remove the anorexia and inability to walk and as a tool to obtain a complete history. The affective component of the illness, namely the depression, was treated with 12 electroconvulsive treatments. Observations to follow remission of the anorexia as related to the number of hypnotic trances, are made (see Figure 1). Also graphic illustrations are presented to show how electroconvulsive therapy affected the trance induction time (see Figure 2).

It would appear that hypnosis is of value in removing the distressing, life-endangering symptoms of anorexia; however, no definite conclusions can be drawn from this one case.

The author wishes to express his appreciation to Dr. W. P. Wilson for his assistance in the preparation of this paper.

REFERENCES

1. Gull, W. W.: *Clin. Soc. Trans. London,* 7:22-28, 1874.
2. Gull, W. W.: *Lancet,* 1:516-517, 1888.
3. Nemiah, John C.: *Am. J. Diag. Dis.,* 3:249, 1958. (No. 4, April.)
4. Wall, James H.: *Am. J. Psychiat.,* 115:11, 1959 (May).
5. Nemiah, John C.: *Medicine,* 29:225, 1950 (No. 3, Sept.).
6. Rolland, C. F.: *Proc. Nat. Soc.,* 12:153, 1953.
7. Cobb, S.: Borderlands of Psychiatry. *Harvard Univ. Press,* Cambridge, 1943.
8. Kay, D. W. K., and Leigh, Dennis: *J. Ment. Sc.,* 100:411-431, 1954 (April).
9. Dubois, F. S.: *Am. J. Psychiat.,* 1949, pp. 106-107.
10. Weidenthal, Daniel T.: *Ohio St. Med. J.,* 55:5, 1959 (May).
11. Noyes and Kolb: *Modern Clin. Psychiatry.* Ed. W. B. Sounders, 1958, p. 464.
12. Cole, Marvin: *Med. Ann. Dist. Columbia,* 25: 605-615, 650, 1956 (Nov.).
13. Gianakon, Harry G.: *J. Kan. Med. Soc.,* pp. 159-163, 1957 (March).
14. Grinshaw, Linton: *Brit. J. Med. Psy.,* 32:44, 1959.
15. Anstreicher, Kurt: *Del. St. Med. J.,* 31:8, 1959 (Aug.).
16. Birnie, C. R.: *Lancet,* II:1331, 1936.
17. Davis, Russell: *Introduction to Psychopathology,* XI:241, 1957.
18. Clark and Willis: *Brit. J. Clin. Practice,* 13:553, 1959 (Aug., No. 8).
19. Eissler, K. R.: *Psychoanalytic Review,* 30:121, 1943.
20. Smith, J. A.: Psychiatry: Descriptive and Dynamic. *Williams & Wilkins Co.,* 1960, p. 123.
21. Yaskin and Brill: Cited by Cole, Marvin. Reference No. 12.
22. Hemphill, R. E.: *Lancet,* II:345, 1944.
23. Sargant, W.: *Lancet,* II:87, 1951.
24. Roth, M. J.: *Electroenceph. Clin. Neudophysiol.,* 3:261, 1951.
25. Kay, D. W. K.: *Proc. Roy. Soc. Med.,* 46:669, 1953.
26. Wall, James H.: *Bull. N. Y. Acad. Med.,* 32:116-126, 1956 (May).
27. West, L. J.: *J.A.M.A.,* 72:6, 128, 1960 (Feb.).

THE HOFHEIMER PRIZE

The prize of $1,500 is awarded annually by the American Psychiatric Association for an outstanding research contribution in the field of psychiatry or mental health which has been published within a 3-year period up to the date of the award. Studies in press or in preparation are not eligible for this award.

This competition is open to citizens of the United States and Canada who were not over 40 years of age at the time the study was submitted for publication; or to a research group whose median age does not exceed 40 years at that time. The next award will be made at the annual meeting of the Association in May 1962. Entries submitted to the Prize Board before March 2, 1962 will be considered. It is imperative that eight reprints or duplicate copies of each entry as well as the necessary data concerning age and citizenship be sent to Peter H. Knapp, M.D., Chairman, Hofheimer Prize Board, Boston University School of Medicine, 80 East Concord St., Boston 18, Massachusetts. All entries are independently evaluated by each member of the Hofheimer Prize Committee and final selection determined by equal vote.

Psychiatric Observations on Juvenile Delinquents in Residential Treatment

SELWYN BRODY, M.D.

Juvenile delinquency is fast becoming a major social disease. Its epidemic proportions appear intimately related to the widespread prevalence of adult delinquency. In fact, the taunt of juvenile delinquency in residential centers has been, on too many occasions, "You adults are more delinquent than *we* are—always promising and never delivering."

Important as the rising incidence of juvenile delinquency is the absence of systematic treatment methods and prevention of this complex syndrome. It is disturbing to realize that no one knows what does cure delinquency.

In this paper, psychiatric observations from seven years as a consultant in residential centers for juvenile delinquents are reported. Not a statistical survey, this study is based upon interviews with over 500 delinquents, therapeutic experience with a smaller number, and conferences with members of allied professions.

Residential treatment, while exploited as an experiment for defeated families, and for authorities to dispose of delinquent youths, actually represents the community's last resort, in many cases, for these individuals to receive treatment. On the other hand, it is a unique facility for psychiatrist and delinquents to be brought together in this special milieu for an extended period.

The role of the consultant in various functions is examined:

(1) Selection;
(2) Diagnosis;
(3) Therapy;
(4) Teaching and training; and
(5) Research.

Selection

The psychiatrist in the screening process helps select youths likely to benefit from residential treatment. He attempts to determine aspects of treatability and reversibility of the delinquent process. In this connection, we have begun to interview the family at intake. However, eloquent psychodynamics do not guarantee prediction. Errors have been made. Experience has shown that individuals "weeded out" as not worthy of treatment may prove to be more responsive than those who had impressed the consultant favorably.

Faced with an ever increasing number of candidates from the juvenile courts, the administration has set the following criteria in keeping with the *limitations* of residential treatment goals:

No murderers or others with a history of extreme violence, or suicidal tendencies are acceptable; fire-setters, overt sex "maniacs" or deviants, overt psychotics, mental defectives are rejected; those with central nervous system disease, such as epilepsy—and those over 15 years of age are finally eliminated. There is the more pressing requirement that the youths on application have at least the semblance of a family (which can be involved in the critical need for family therapy) to whom the youth can be returned upon discharge.

Diagnosis

From clinical and psychological studies, conviction grows that delinquents rarely suffer from mild emotional disorders. The delinquency syndrome expresses a life preservative function for the release of intolerable tensions.[1] The form of the sickness represents the only way by which the majority can ever get help.

Menninger's statement on the behavior disorders[2] is pertinent:

"A name is not a diagnosis. It does not determine treatment. Its net effect has come to be that of destroying hope. Our impressive psychiatric labels freeze a phase of the

Presented at the 1960 Annual Meeting of Am. Ortho. Assn., Chicago, Ill.

From Psychiatric Dept., Children's Village, Dobbs Ferry, N. Y.

process. They misrepresent and they strike a blow at hope and hence at treatment."

There is an urgent diagnostic need to understand the interaction between delinquency and psychosis or depression. A large number of these children are disturbed adolescents who are more borderline or psychotic[3] than delinquent. Their roots are sick, their foundation poor, though often presenting an appearance which may be deceptively attractive.

Current screening favors an increased number of so-called "unsuccessful" delinquents. This type is not the case-hardened, "normal" delinquent. The veneer of defiance and self-confidence is thin. Few are from organized gangs; rather they are truants who have committed minor crimes alone or in small groups. The majority are lonely, unappealing, friendless failures, often dull with severe learning problems; self esteem is minimal.

Therapy

Treatment is the reason-for-being of the residential institution. Here we are challenged by formidable problems. The residential population may be roughly divided into three groups. Actually, sharp lines do not stand up to scrutiny and overlapping makes statistical figures not too useful.

(1) The first group consists of those in whom a favorable response to environmental and individual therapy occurs. Super-ego development and reaction formation are essential factors in their progress. Improved behavior contributes to a better self-image. Follow-up studies determine the permanence of improvement.

(2) The "unsuccessful" delinquent, who is accessible to adults and on whom "a dent can be made," is considered available for therapy. But he may regress, when he feels pressure towards yielding the dependence which he has never had consistently gratified. In such instances he may reveal a whining, sticky behavior—or panicky withdrawal. If he is not penalized by transfer to a mental hospital, two years of therapy becomes a virtual drop in the bucket.

(3) The so-called "normal" delinquent troubles the milieu far less. He is a "treatment rejector,"[4] who feels above and beyond needing help. He is pseudo-mature, controlled and his masculine self-image precludes confiding in therapists. He "plays it cool" for time, adroitly adjusts to the residential structure, or milieu. On him "no dent has been made." It is hoped that two or three years of residential containment will rub off on his ego surface, even if his basic personality is unchanged. However, the evidence indicates that his psychopathy is strengthened by his two years of successful manipulation of the staff, which more often than not has played into his hands. Consequently, he is the one most likely to make the front pages with capital crimes. The limited goal of containment is seriously questioned.[5]

The paucity of teachable methods contributes to the treatment dilemma for juvenile delinquency. No one knows what cures delinquency. Exponents of reliance upon milieu for progress are warned by Redl[6] against naive overexpectations. For individual therapy, it is equally magical to depend on psychoanalytic formulations.[7-9] An additional handicap is the dearth of workers and consultants experienced in the therapy of delinquents.

Despite imposing difficulties, there are rewarding experiences. It has become a challenge to find some means of reaching the human being who has been classified as "unanalyzable," and we must accept the need for parameters with delinquent patients.

Sometimes the therapist's most reliable ally is the patient himself. Beneath the smoke and noise lie the youngster's unconscious ego ideals, his wish to like, respect, trust others and his desire for the reciprocal treatment. In building a relationship we sometimes have to act as a frustrating, depriving disciplinarian. Actually, the disturbed adolescent can initially find great comfort in regarding his therapist as an unreasonable tyrant.[10]

We may learn also from the work of Weinrib,[11] who states, "In confronting the ego of the impulsive adolescent we seem to impress

him that we are strong and helpful, and can help him learn control over his frightening but tempting impulses." Weinrib claims that unwilling youths have thereby become involved in a meaningful therapeutic relationship.

Psychoanalytic modifications I have found to be effective in therapy and teaching include:

(1) *Supportive therapy* with emphasis on warmth and positive relationship has the widest application, of course.

(2) *Reinforcement of defenses* based on the principle of joining forces with the delinquent. Through this technique, the attempt is made to help him outgrow his symptomatic defenses.

In one case, treated individually once a week for a period of three years, there was dramatic redirection of a blustering, bullying exterior to the underlying personality of a shy, weak, self-conscious boy. In quietly standing his ground, the therapist gradually was able to uncover (and reinforce) the patient's basic defense, which hardly could have been observed as a defense. Beneath the shouted abusiveness, the patient's wish to be better controlled was his essential defense. The therapist chose to join forces with this fundamental wish, rather than with the more obvious outwardly expressed wish, his overt defense, his apparent desire to be a "bigshot."

These deprived, hostile boys have the frustration tolerance of a sensitive and hurt two-year-old child. And yet, the therapist's quiet refusal to "budge an inch" when being on the receiving end of the verbal attacks acted as a kind of frustrating, not of the attacks themselves, but of their efficacy. When patient had had his fill of being allowed to verbalize his rebellion against the very treatment itself: "Give me a *rush* job—I have no time for this nonsense—I am no psycho," etc.—all in the loudest, rudest tones; when he learned that no acting out was permitted, only verbal behavior, he reacted to the reality frustration of his attempt to be a "big shot." He could come to the end of his bluff and get down to his real need for a more positive relationship, and reveal his deeper wish to have better control of himself. It was the therapist's recognition of this deeper need and his "joining forces" with it that enabled patient to come to treatment with expression of his mass of fears—regarding his appearance, his intelligence, his sanity, etc. He shed his swagger and began to talk about his family life and his inner feelings.

(3) The technique of *reflecting negative patterns*[12] encourages the ego to discharge hostility verbally. One of the most difficult problems is that of the non-verbalizing delinquents. Occasionally such youths can be helped by the therapist's mirroring his silence. One such patient said, "Why don't you ask me questions?" The reply, "When I did ask you, you didn't answer anyway, so why don't we both just be quiet? Didn't you ever sit quietly with your parents?"

This evoked an interesting area of conversation and enhanced the therapeutic relationship. Another boy, who mumbled and whimpered, was echoed[13] by a kind of mocking of his negative behavior. He finally got angry. He overcame his ineffectual exterior and related that he was an expert at building model airplanes. He said he could even spell Mississippi.

Another boy who said he was no good at making friends, no good at reading, no good at sports—the therapist mirrored thusly, "You're good at getting people discouraged." The boy's response was, "You'll have to be *very* good not to quit on *me.*"

The techniques of *reinforcement of defenses* and *reflecting negative patterns* are specialized extensions of ego-strengthening procedures, advocated by Spotnitz.[14] They augment the therapist's devices for treating the delinquent when a positive relationship cannot be sustained.

(4) In the treatment of these youths, there is an *induced delinquency* syndrome in which delinquency patterns are aroused in the therapist. The assignment of roles is a critical factor in this process. The phenomenon is similar to neurosis and psychosis induced in the therapist treating such disorders.[15]

When this induced delinquency is effectively exploited by the patient, his deviant behavior is enhanced. When successfully conducted by the therapist, he defeats the delinquency at his own game; the result is control of delinquency, reminiscent of Aichorn's method, particularly as elaborated by Noshpitz.[16] Intensive research is required for the exploration of this technique.

(5) The dramatic interest of psychiatry in the family is reflected in the residential centers.[17] Therapists are being assigned to treatment of the family of the residents. This constitutes a gain in restoring delinquents and their families. It should be added that without involving treatment of the family, improvement of the juvenile delinquent has, upon occasion, acted as a destructive factor in the relapse of parental delinquency.

(6) Group psychotherapy and aftercare services are being expanded.

Conclusion

It is recommended that:

(1) The more modern methods of psychoanalytic psychotherapy, based upon joining, rather than attacking or analyzing defenses, be made available to delinquent youths, whether they have been classified as "inaccessible" or not;

(2) That consultants experienced in these procedures teach them to the therapists.

Seven years of exploration has indicated that worthwhile results may be obtained with seemingly hopeless subjects by the intensive application of ego strengthening techniques.

2 East 86th Street, New York 22, N. Y.

REFERENCES

1. Glover, E.: "'Functional' Group of Delinquent Disorders," Chapter 25, p. 379, "On the Early Development of Mind." *Intl. Univ. Press,* 1956.
2. Menninger, K. M.: Hope; The Academic Lecture. *A.J.P.,* 116, p. 481, Dec. 1959.
3. Glover, E.: The Analyst's Case List, "Psychopathic Delinquency," p. 221, The Technique of Psychoanalysis. *Intl. Univ. Press,* 1955.
4. Brody, S.: Syndrome of the Treatment Rejecting Patient. *Presented at APA Meeting,* San Francisco, 1958. To be published.
5. Hendrickson, W. J., et al.: Psychotherapy with Hospitalized Adolescents. *A.J.P.,* 116, p. 527, Dec. 1959.
6. Redl, F.: The Concept of a Therapeutic Milieu. *A. J. Orthop.,* 29, p. 721, Oct. 1959.
7. Eissler, K. R.: Problems of Technique in the Psychotherapy of Adolescents from *Psychoanalytic Study of the Child,* Vol. 13, p. 223.
8. Ibid.: Effect of the Structure of the Ego on Psychoanalytic Technique. *J. Psa. Assn.,* 1, p. 104, 1950.
9. Josselyn, I. M.: Psychotherapy of Adolescents at the Level of Private Practice. Psychotherapy of the Adolescent, Balser, Ed., p. 32. *Intl. Univ. Press,* N. Y.
10. Hendrickson, W. J., et al.: *Loc. Cit.* (No. 5, above.)
11. Weinrib, J.: Impulsivity in the Adolescent and Its Therapeutic Management. Paper No. 102; p. 109 Summaries of Papers. *A.P.A. Annual Meeting,* 1959.
12. Glover, E.: *Loc. Cit.* (No. 3, above, p. 225).
13. Spotnitz, H., et al.: Ego Reinforcement in the Schizophrenic Child. *A. J. Orthop.,* 26, p. 146, Jan. 1956.
14. Ibid.: Strengthening of the Ego Through the Release of Frustration-Aggression. *A.J. Orthop.,* 28, p. 794, Oct. 1958.
15. Searles, H. F.: The Effort to Drive the Other Person Crazy—An Element in the Etiology and Psychotherapy of Schizophrenia. *B. J. Med. Psych.,* 32, pp. 1-18, Post 1, 1959.
16. Noshpitz, J.: Opening Phase in the Psychotherapy of Adolescents with Character Disorders. *Bull. Menn. Clinic.,* 21, p. 153, July 1957.
17. Ackerman, N. W.: The Psychodynamics of Family Life. *Basic Books,* 1959.
18. Engel, M.: Shifting Levels of Communication in Treatment of Adolescent Character Disorders. *Arch. Gen. Psych.,* 2, p. 94, Jan. 1960.
19. Eissler, K. R., editor: "Searchlights on Delinquency." *Intl. Univ. Press,* 1949.

CORRECTION

In the September 1961 issue of *Diseases of the Nervous System* the name of the principal author of the article "High Dosage Hydroxyzine in Institutionalized Mental Patients" was misspelled. The authors of this paper are Anthony Lapolla, M.D., and Jesus Iberra, M.D.

Effect of Chlorprothixene on Schizophrenic Patients

ALBERT A. KURLAND, M.D., and ESBER YAZICIOGLU, M.D.

Introduction

The therapeutic success of chlorpromazine in psychiatric treatment provided a powerful stimulus for the development of more potent congeners. This has led to a continuing series of modifications of the phenothiazine structure. There were modifications in the side chain and a series of phenothiazine derivatives were synthesized which yielded more potent compounds dosagewise. This was followed by alterations in the central structure yielding a compound such as imipramine (Tofranil), resulting in a changing spectrum of therapeutic effects in psychiatric patients.

These considerations have led to continuing studies of such modified compounds as chlorprothixene (Taractan) having the formula 2-chloro - 9 - (3-dimethylaminopropylidine)-thioxanthene which appeared particularly interesting on the basis of the pharmacological data[1] obtained in animal screening studies. These studies indicated that while chlorprothixene had certain similarities to chlorpromazine, it was less toxic. In addition it had the property of being less likely to produce catatonic states in rats. This appeared to be an important consideration since the catatonic producing effect of a variety of phenothiazine derivatives administered in high dosage in animals had been correlated with a tendency to produce parkinsonian effects in man.[1] The question therefore arose whether this compound might produce the effects of chlorpromazine without its neurological complications.

Clinical studies were initiated by Madsen and Ravn[2] and Kruse[3] who reported favorable results, describing the compound as having effects similar to chlorpromazine as well as having the additional effect of being an antidepressant. This rather interesting combination of psychiatric effects reported in this drug stimulated an exploratory clinical study at the Spring Grove State Hospital.

Methodology

This study comprised 25 white female patients ranging in age from 22 to 64 years residing on the closed wards of a chronic service in the Spring Grove State Hospital. These were wards having large numbers of patients and relatively few personnel. Of these, 23 were diagnosed as schizophrenic reactions and two as depressions (Table I). These patients had been on drug therapy of one type or another continuously or intermittently in attempts to bring about some symptomatic improvement in their behavioral disturbances.

Prior to the initiation of treatment with chlorprothixene all current medications of these patients were discontinued. There were only four cases in which the drug free interval exceeded 30 days (Table I). Prior to the initiation of treatment a urinalysis, WBC and hematocrit were obtained and repeated every two weeks while the patient was on the drug therapy. Weekly determinations of weight and blood pressure were made.

This being an exploratory study no attempt was made to carry out a blind or double blind technique. The patients were known to the psychiatrists (A.A.K. and E.Y.) and were seen independently by each several times weekly. When treatment with the experimental drug was terminated the observations were compared. No significant differences were observed in these comparisons.

Observation was commenced prior to the discontinuance of previous drug therapy. The patients were seen at regular intervals through the drug free interval, during the treatment phase ranging from 25 to 35 days and during the post drug treatment period of two to three weeks.

The dosage consisted of a starting daily dosage of 25 mg. t.i.d. administered orally for 5 to 10 days, then increased to 50 mg.

From Research Department, Spring Grove State Hospital, Baltimore, Md.

The drug, chlorprothixene, used in this study, was made available as Taractan (Ro 4-0403) by Hoffmann-La Roche Inc., Nutley, N. J.

b.i.d. for 5 to 7 days. This was then increased to 50 mg. t.i.d. for 21 days providing a total period of medication of 35 days. As our experience with this drug increased the regimen was altered on the final six patients in the study by intensifying the drug administration. This consisted of administering 25 mg. t.i.d. for 5 days; 50 mg. b.i.d. for 5 days; 50 mg. t.i.d. for 5 days and 50 mg. q.i.d. for 10 days.

Results

Table I indicates the response of the patients. It may be observed that there were only five patients—Cases Nos. 2, 7, 8, 11 and 17 that showed a degree of improvement that could be considered moderate as indicated by some degree of behavioral change. Except for Case #7, they were not sufficiently improved, however, to be considered for transfer to a better ward.

TABLE I

Response to Chlorprothixene

Pt.	Diagnosis	Age	Hosp.-Yrs.	Drug Free Interval (Days)	Result	Side Effects
1.	Undifferentiated	29	7	12	W	
2. (D)	"	35	17	20	+	Headache
3.	"	42	26	18	0	
4.	"	42	28	30	W	
5.	"	43	22	12	†	
6.	"	49	17	77	0	
7. (D)	"	56	4	35	+	
8.	"	57	26	11	+	Headache
9.	"	64	13	12	0	and vom-
10.	Paranoid	22	7	20	W	iting
11. (D)	"	23	6	35	+	
12. (D)	"	31	13	7	0	
13.	"	36	3	2	0	
14.	"	43	1	135	W	
15. (D)	"	49	24	7	0	Sleepless-
						ness
16.	"	52	3	11	W	Headache
17.	"	63	17	11	+	
18.	Hebephrenic	27	7	12	0	
19.	"	31	7	12	0	
20. (D)	"	32	9	8	0	
21.	"	37	20	12	0	
22.	"	40	7	12	0	
23. (D)	Depression	55	4	8	0	
24. (D)	"	68	1	8	0	
25. (D)	"	55	28	18	W	Sleepless-
						ness

+ = Moderate improvement; † = Minimal improvement; 0 = No change, and W = Worse. (D) = Indications of depressive symptomatology.

Case #2. Patient displaying moderate behavioral improvement.

A 35-year-old white female patient hospitalized since 1943. Her schizophrenic pattern gradually changed from catatonic to a relatively undifferentiated type. She is usually apathetic and withdrawn. At times she will use excessive make up giving herself a weird appearance and will wear a great deal of costume jewelry. Her affect for the most part is flat although at times she seems depressed. Her response to questions is in a childlike manner and irrelevant. Her verbalizations indicate confusion and disorganization. She spends time lying on the floor overtly masturbating. In the past she has had several courses of ECT and in recent years various regimens of drug therapy with little benefit.

The patient was placed on chlorprothixene and no change was noted the first week of treatment. Subsequently, she began to complain of headaches, which were unusual for her. However, she seemed to become somewhat less withdrawn, more talkative and there were less manifestations of sexual activity. Some improvement in her behavior was noted. Two weeks after medication was discontinued, her condition remained unchanged.

Since the compound had been described as having antidepressant activity, all the cases in this study where there were some manifestations of depressive symptomatology were evaluated as to the effect in this area. These were cases 2, 7, 11, 12, 15, 20, 23, 24, 25 (see Table I). Of these there were only three (Nos. 2, 7, and 11) out of the 9 cases who showed a degree of improvement which could be considered moderate.

Case #7. Patient displaying moderate improvement especially in the area of depressive symptomatology.

A 56-year-old white female admitted in 1956 with a diagnosis of chronic brain syndrome with psychotic depressive reaction. Later a pattern resembling undifferentiated schizophrenic reaction emerged. She remained tense, apprehensive with much psychomotor retardation. Frequently there would be episodes in which she would appear very depressed and agitated. She soils often and remains isolative. Attempts to interview her were unproductive since she answered only briefly or not at all. In spite of this she gave the impression of being alert, aware of what was taking place but was unable to relate

because it was too threatening to her. In her past she had received ECT with various courses of drug therapy, tranquilizers and antidepressants, with no particular effect.

During the first week of chlorprothixene therapy she showed some change in her general behavior and habits. She stopped soiling, became more relaxed, and started to gain some weight. As treatment continued she seemed to show signs of being less retarded, slept better and showed occasional moments of cheerfulness. Two weeks after the drug was discontinued she started to regress. She was placed back on drug therapy with some improvement and arrangements were made to transfer her to a better ward.

There were 13 patients who showed minimal or no change. These were cases Nos. 1, 3, 6, 9, 12, 13, 15, 18-24. There were six cases Nos. 1, 4, 10, 14, 16, and 25 who appeared to get worse as indicated by some exacerbation of their symptomatology.

There were relatively few complications observed. These were an episode of vomiting in one patient, two patients complaining of headache and two of sleeplessness.

Discussion

The relatively few cases in our study demonstrating a response which could be considered moderate were at variance with the reports of Madsen and Ravn[1] which indicated that 62 per cent of schizophrenic patients treated with the compound showed a favorable response. Kruse[3] reported faforable results in a group of 30 female patients. Of these, 10 were manic-depressives; 8 involutional depressions, 6 schizophrenics with marked and persistent depressive features and 6 were reactive depressions of the psychoneurotic category. Eleven of the 30 patients showed excellent response and were able to leave the hospital on extended visits. The seven acute cases (6 psychoneurotics and 1 manic-depressive) responded better than the chronic ones. Only five (2 manic-depressive and 3 involutional depressives) of the 23 chronic cases could be classified as excellent results. As to dosage, Kruse stated that a few patients responded satisfactorily to dosage of 100 mg. daily; most of them needed 150 mg. Further increases up to 400 mg. daily helped only in two cases and did not help in six.

This difference in result may have been due to the more chronic nature of our patients. It may be due also to the fact that ours is a group of patients who have remained in the hospital as treatment failures in spite of exposure to a variety of drug therapy regimens. Whether higher dosage would have been more effective seems unlikely since other investigators[4] studying this compound have not observed a greater therapeutic effect with high doses. It is the impression of these investigators that the antipsychotic and antidepressive effect of this compound in chronically ill schizophrenic patients is of a minimal nature. It does not seem to offer any advantages over the drugs already available in this area of treatment.

Conclusion

Chlorprothixene administered in a dosage range of 100 to 200 mg. daily to 25 chronically ill schizophrenic patients over a 4 to 5 week period brought about a symptomatic improvement which could be considered moderate in 20%; minimal or no change in 56% and some intensification of the existing symptomatology in 24%. On the basis of these findings in the dosage employed the value of this compound as an antipsychotic and antidepressive agent in the chronically ill psychotic patient is considered to be of a minimal nature.

Acknowledgments: This study was made possible by a research grant and supplies of chlorprothixene (Taractan—Ro 4-0403) by Hoffmann-La Roch Inc. This grant was administered by Friends of Psychiatric Research, Inc. Appreciation is expressed to Dr. Bruno Radauskas, Superintendent, Spring Grove State Hospital for making clinical facilities available.

BIBLIOGRAPHY

1. Data supplied by Roche Laboratories.
2. Madsen, E., and Ravn, J.: Preliminary Therapeutic Experiments with a New Psychotropic Drug. *Nord. Psychiatr. tidsskr.*, 13:82, 1959.
3. Kruse, W.: Preliminary Report on a New Psychotropic Compound (RO4-0403/W). *Am. J. of Psychiat.*, 116:849-850, March 1960.
4. Personal communication, Dr. Herman C. B. Denber, Manhattan State Hospital, N. Y. City.

A Clinical Trial Study of Trifluoperazine

NINA KATERYNIUK, M.D., and CHARLES W. MORRIS, M.D.

Introduction

Stelazine, a brand of trifluoperazine, is one of the most potent phenothiazine compounds available at the present time. According to numerous publications, it is more effective in small doses, has a more rapid onset of action and a more intense effect on various psychotic symptoms. Stelazine is reportedly about 10 times as potent as chlorpromazine, measured in terms of tranquilizing activity. There is a narrow range between the therapeutic doses of this drug and the slightly higher ones which may cause untoward side effects. Its therapeutic value is motivated by the idea (based on experimental study and clinical observations) that the more potent the phenothiazine derivative, the fewer side effects it produces. Although the side effects of Stelazine still present an area of serious consideration and require special management, no reactions such as agranulocytosis or jaundice were reported in clinical use of the drug. In comparison with other phenothiazine derivatives, Stelazine is said to have less sedative and hypnotic properties. It is recommended for treatment of all types of psychotic disorder, however, with an emphasis that Stelazine acts specifically and rapidly to bring about the disappearance of hallucinations and delusions. It is also supposed to aid in activating withdrawn, resistant and lethargic patients. The treatment of patients must be individualized and the physician must be prepared to deal promptly with Stelazine side effects (Parkinson reactions, dyskinetic syndromes, and akathisia). A great deal of the success with Stelazine treatment depends upon the physicians' knowledge of when and how to administer it properly.

Sixty-six patients, 31 men and 35 women were studied at Central State Hospital in regard to their progress during Stelazine treatment. Age varied from 17-77 years. The period of time considered extended from 12-293 days.

The following table is an analysis of the group according to the number of patients, the dosage, and duration of Stelazine treatment:

Month	No. of Patients	Dosage
1958 December	2	15 mg.
1959 January	4	15 mg.
February	1	15 mg.
March	0	
April	3	20 mg.
May	7	11 mg.
June	4	25 mg.
July	9	19 mg.
August	20	17 mg.
September	16	20 mg.

Of these patients 59 were continued on Stelazine until September 30, 1959, the ending time of the study. The other seven patients were taken off the drug before that date.

Diagnostic categories represented in the group included:

Diagnosis	Male	Female	Total
Schizophrenia	25	32	57
Psychoneurosis	1	1	2
Involutional Psychotic Reaction		1	1
Manic Depressive Psychosis		1	1
Mental Deficiency with Psychosis	2	0	2
Chronic Brain Syndrome Associated with Organic Brain Disease	3		3
Totals	31	35	66

Method of Study

The group of female patients was selected at random, every other name from our total list. The male patients, selected in no particular order, represent about 85 per cent of the total male list.

In addition to assessment of each patient's progress as described later, patients' records or follow-up summaries were examined concerning the following:

1. Length of time of Stelazine administration.
2. Daily and total dosage (average calculated per month).

From Central State Hospital, Lakeland, Ky.

3. Other medicines and treatments concomitant with Stelazine treatment.
4. Tolerance of drug with special attention to side effects.
5. Any reason for termination of Stelazine treatment.

The senior investigator discussed, personally, with the attending physicians the progress of each of the 66 patients in the study. These main points received particular consideration in the discussion: 1) reason for choice of Stelazine, 2) general impression as to the therapeutic action of Stelazine, based on physician's own experience.

As is shown in tabulation of diagnostic categories, the great majority of patients consisted of schizophrenics. With only two exceptions, all of the patients had histories of prolonged hospitalization and belong to the chronic population of our hospital. Before Stelazine treatment, they had been treated with other psychotropic drugs or by methods such as electroshock, psychotherapy, general hospital care, etc.

The choice of Stelazine treatment was motivated primarily by the subjects' unsatisfactory response or failure to improve on previous treatment. The evaluation of patients' progress was done by comparative study of the symptomatology manifested before, during, and at the end of Stelazine trial.

The main area of attention centered on patients' behavior, attitudes, emotional status, content of thought, sleep and appetite.

Classification of the Types of Responses:

I. *Significant favorable changes* resulting in lessening or disappearance of undesirable symptoms during the course of Stelazine treatment were classified as follows: a) "markedly improved" the term involves change from pronounced deviation in one or more of the areas cited, with socially inappropriate behavior, to a state in which the patient's social behavior was appropriate (and sustained for a month or more); b) "improved" implies decrease of severity of symptoms with subjective "feeling better" and better adjustment to the routine management; c) "slightly improved" indicates amelioration of certain symptoms only (such as insomnia, etc.) without obvious change in the clinical picture as a whole.

II. *Unfavorable response* includes "no change"—i.e., no essential change in the symptomatology, lack of improvement or worsening of patients' condition during Stelazine treatment (exceeding 2 weeks trial) is classified as follows: a) "doubtful"—uncertain or fluctuating improvement with transient short periods of diminution of some disturbing symptoms; b) no essential change; c) "worse"—exacerbation of symptoms and/or development of new undesirable symptoms.

Results obtained are enumerated in the following tables:

Favorable Response:	
Markedly improved	5
Improved	3
Slightly improved	17
Total	25
Unfavorable Response:	
No change	15
Worse	5
Total	20
Doubtful	21

No discernible relationship was observed to exist between diagnostic categories and individual response to Stelazine.

Discussion

A group of 66 patients, predominantly chronic schizophrenics, were treated with Stelazine at Central State Hospital for a period ranging from 12 to 293 days. Of these patients 25 responded favorably; the therapeutic effect in 41 other patients was negative or doubtful. Ten patients from the total group began to manifest severe side effects such as Parkinson's syndrome, difficulty in swallowing, drowsiness, extreme restlessness, irritability and akathisia. Artane, Cogentin and occasionally barbiturates were required as supplementary treatment to control the symptoms. Eight schizophrenic patients showed marked transient reactivation of psychotic manifestations during the initial period of Stelazine treatment. These patients' final responses justified their classification as "improved." Three patients showing satisfactory responses to Stelazine re-

fused to take the medicine because of a subjective feeling described as extremely upsetting and contributing to patients' restlessness or insomnia. In five patients classified after their progress as "worse," Stelazine was discontinued after the undesirable symptoms (reactivated psychosis), persisting over a period of 10 to 12 days, could not be controlled by addition of sedatives. All of these patients were later helped by electroshock treatment.

One physician taking care of geriatric patients observed that old schizophrenic patients became more communicative on Stelazine treatment. Some of these patients who remained, as a rule, in the back of the ward, and completely withdrawn from their surroundings, began to move around, ask questions and participate in group activities. When these patients were temporarily taken off Stelazine on a few occasions (no supply available), they asked the physician for "the medicine." Other physicians felt that although some of their patients showed most remarkable improvement on Stelazine treatment, these subjects had responded similarly to other psychotropic drugs, notably chlorpromazine.

No allergic skin manifestations were observed among the subjects treated with Stelazine.

REFERENCES

1. Wright, J.: Newer Phenothiazine Drugs in Treatment of Nervous Disorders. *J.A.M.A.*, July 11, 1959, Col. 170, pp. 1283, 1288.
2. Payne, P.: Trifluoperazine in Treatment of the Acutely Ill Psychotic. *Can. Med. Assn. J.*, July 1, 1959.
3. Ayd, F., Jr.: Current Status of the Phenothiazine Tranquilizers. Transactions of the Fifth Annual Meeting, *Acad. of Psychosomatic Medicine*, 1958.
4. Brill, H.: Trifluoperazine, Clinical and Pharmacological Aspects." *Lea & Febiger*, 1958 Edition, Philadelphia.

An Unusual Reaction to an MAO Inhibitor

J. TUPIN, M.D.

Psychopharmacology and its clinical application has made great strides in the last decade. There is little room for doubt that this is the area that offers the most promise of rehabilitating our vast number of psychiatrically ill. The rapidity with which new drugs have appeared is astounding and, as yet, we have but scanty knowledge of their mode of action, benefits and toxicity. For example, the monoamine oxidase inhibitors only recently have had wide spread clinical usage in psychiatry and presentation of this case affords an opportunity to review some of the pertinent literature and point out a possible serious side effect to one, phenelzine.

Case: I.D., a 45-year-old white married female was admitted to the hospital on September 23, 1960, with unilateral, idiopathic paralysis agitans and a variety of depressive manifestations.

Her illness began one year prior to admission with right sided muscular rigidity, cramps in right calf and shoulder, stooped posture, shuffling slow gait with the right arm carried in a flexed, fixed position, and slow deliberate speech. Minimal confusion and recent memory disturbance had been noted by the family, as well as restricted thought content and extremely repetitious conversation. These symptoms showed moderate, steady increase with but transient improvement on various medications.

Shortly after the onset of her illness, she experienced decrease in appetite, loss of interest, and had periods of crying. When she was admitted these were accentuated and she was also expressing self depreciatory ideas. A diurnal mood swing and a sleep disturbance were noted at that time. She denied thoughts of suicide. There was no history of hypertension, cardiovascular disease, central nervous system infection, or trauma. Family history did not reveal similar illnesses.

On admission it was noted that she cried frequently with apparently depressed affect, expressing ideas of unworthiness, ate poorly, and presented a poor sleep record.

From The Department of Neurology and Psychiatry, University of Texas Medical Branch, Galveston, Texas.

The general physical examination was within normal limits.

Neurological examination revealed a slow deliberate gait, decreased right arm associated movement, right sided passive resistance, plastic rigidity with cogwheel phenomenon in both right upper and lower extremities. Additional findings were: bilateral ankle clonus, right lower extremity spasticity, nonrhythmical coarse bilateral tremor, hyperactive deep tendon reflexes, bilateral Hoffmann's reflexes; great toe extensor responses were equivocal. The remainder of the neurological examination was within normal limits.

X-ray of the skull and chest were normal. The EKG revealed frequent PVC's as a trigeminal rhythm and negative T waves in V_1-V_3. She had a normal waking and sleep EEG. Routine urinalysis, CBC, Serum Bromide, BUN, and Cholesterol, were within normal limits. L.E. preparations and Schwartz-Watson studies were negative. PBI was 6.3 micrograms per cent. CSF studies were normal except for the protein, which was 82 mg.%.

One week after admission, October 1, 1960, she was started on phenelzine, 30 mg. t.i.d. Subsequently, on October 5, 1960, she was given phenoxene, 50 mg. b.i.d. She received no other "suspect" medications. This was continued with no apparent change until the afternoon of October 12, 1960, twelve days after phenelzine was begun, when she was noted to have an elevation in temperature which over the next 24 hours gradually increased to 107.2 degrees, rectally. At the outset she exhibited increased patellar and ankle clonus, bilateral Babinski responses, confusion to semi-stupor, urinary incontinence, tachypnea, and profuse perspiration. Her pupils were moderately contracted and reacted to light. The remainder of the physical examination was normal and no evidence of infection was found. Within 18 hours the previously increased muscular rigidity progressed to the point of bilateral boardlike, extensor spasm with mild opisthotonos and trismus. This lasted 24 hours and then gradually subsided. She was totally unresponsive during this time. Her pulse was never above 120 and her blood pressure was normal throughout the episode.

Laboratory studies during this acute phase consisted of cerebrospinal fluid analysis, serum electrodytes, blood counts, serum calcium and phosphorous, blood urea nitrogen and urine analysis. These studies were not remarkable and all were within normal limits except for the cerebrospinal fluid protein which continued to remain above 80 mg.%, and a minimal increase in the CO_2 combining power.

Management included antipyretics, ice packs, alcohol sponging, antibiotics and intravenous fluids. Temperature was kept below 105 degrees with these measures and began dropping in 12 hours. It returned to normal levels in 48 hours, and she became responsive and with fair orientation. Energetic fluid administration, consisting of 6500 cc., was necessary to balance the perspiration losses the first 24 hours. In spite of this large fluid intake, her urine output remained less than 250 cc. during that time. We felt this was because of the massive losses via perspiration; 72 hours after the onset she again became disoriented, experienced bizarre visual hallucinations and increased depressive symptoms. This lasted 24 hours.

An arteriogram performed on October 14, 1960 was normal. No relaxation occurred with the general anesthetic. (For completeness, a pneumoencephalogram was done on October 25, 1960 and was normal.)

The rigidity, depression, and confusion gradually subsided, and she was restarted on phenoxene, 50 mg. twice a day, which was increased to 50 mg. four times without incident to date of dismissal two weeks later. There were no sequelae and she was essentially as she had been on admission.

Since the discovery of monoamine oxidase by Hare[1] in 1928, there has been continuous interest in its physiological action.[2] It has been repeatedly demonstrated to be active in the oxidation of various amines. It has been studied with interest, especially in the metabolism of 5-hydroxytryptamine,[3,4] epinephrine[5] and norepinephrine.[6] It is found in the brain with the hypothalamus exhibiting the highest concentration.[7]

Iproniazid was one of the earliest potent monoamine oxidase inhibitors,[8] and certainly has been studied more exhaustively than any other. Therefore, some inferences will have to be drawn from its actions, since some of the data are not yet available on phenelzine. Repeated demonstrations of its effectiveness *in vivo,* have been made.[9-13] Also, many other compounds, including phenelzine,[14] are known to be active *in vivo.*

Shore[12] demonstrated increases of serotonin and norepinephrine in the rabbit brain after a large single dose of iproniazid and prolonged administration of smaller doses. Phenelzine increases the mouse brain serotonin content, and Chessin[14] pointed out that activity was present for one to three weeks after a single dose. A parallel decrease in the monoamine oxidase activity was noted. Iproniazid shunts epinephrine into an alternate metabolic pathway[15] and increases the amount excreted in the urine.[16] There is evidence that some actions of epinephrine are not potentiated.[18]

Although serotonin does not cross the blood-brain barrier, its precursor, 5-hydroxytryptophane (5-HTP)[19] does.

Potentiation of the central pyretogenic and stimulation effects of 5-HTP and DOPA has been reported with both iproniazid[9-17] and JB-516 (PIH).[14]

Studies[20] of the effect of 5-HTP on dogs and cats, following administration of iproniazid, revealed tremor, increased resistance to passive movement, sympathetic stimulation, extensor twitches, rigid plastic extension, sedation following initial stimulation, and increase in nasal, salivary and lacrimal secretions. Acute toxicity of phenelzine[14] in mice was characterized by CNS stimulation, with hyperactivity, piloerection, salivation, lacrimation and convulsions. It should be pointed out that inhibition of monoamine oxidase potentiates certain drugs.[21] Epinephrine increases the rigidity and exaggerates the tremor of parkinsonism by an unknown central action.[22]

Davis[23] has grouped the toxic reactions of monoamine oxidase inhibitors into three classifications.

1. Overstimulation of mental and physical activity.
2. Potentiation of drugs.
3. Liver toxicity.

Clinical studies have reported side effects of phenelzine[24-28]:

Anemia, leukopenia, rash, constipation, hypotension, transient impotence, nausea, warmth, dry mouth, ankle edema, hypernatremia, drowsiness, dizzyness, ataxia, euphoria, overactivity, vomiting, muscular stiffness, profuse perspiration, excitement.

Sainz[27] has noted that phenelzine is toxic in doses greater than 50 to 75 mg. orally four times daily. The entire syndrome of hyperepinephrinemia is produced at that level. One of the earliest reports of toxicity to monoamine oxidase inhibitors was by Susbac[29] who was using iproniazid as an antituberculous agent. He had two cases which at the time of induction of general anesthesia exhibited hyperreflexia, clonic muscular contractions, bilateral Babinski responses, tachycardia, hyperventilation and temperature to 106.5 degrees. A subsequent report[30] of toxicity noted agitation, delirium, clonic convulsions, hyperthermia, flushed face, dry skin and dilated pupils. These symptoms followed the intramuscular injection of 25 mg. of imipramine hydrochloride in a patient who was taking phenelzine. A suicide attempt[31] in which twenty-five 15 mg. tablets were taken resulted in dilated pupils, delirium, restlessness, progressing to semicoma, hyperflexia, muscular spasticity, trismus, excess salivation, and urinary incontinence.

Discussion

The production of the picture seen in this case may have been due to several interacting factors. It is necessary to consider the precursors of serotonin and epinephrine, as well as these substances themselves as producers of the symptoms. In addition, alternate pathways of metabolism that come into use when monoamine oxidase is blocked, make it possible that a metabolite not ordinarily in the brain may have been responsible. Since it is known that parkinsonism is aggravated by epinephrine, and much of our patient's picture was an exaggeration of her previous findings, it is reasonable to surmise that the parkinsonism was a predisposing factor. The possibility that organic brain disease involving other areas, may have a similar effect, should also be kept in mind.

The concomitant administration of other drugs is known to produce severe reaction. There is the possibility that phenoxene contributed to the reaction in some way but it seems unlikely. It certainly should be emphasized that inhibition of monoamine oxidase potentiates the action of numerous drugs. Reserpine is known to release serotonin and epinephrine in the brain and to produce excitement following monoamine oxidase inhibitors and, therefore, should be used cautiously with them.

Finally, it seems that administration of phenothiazines, known serotonin antagonists, might be helpful in the management of similar reactions.

Author's Note: I am indebted to Dr. Hamilton Ford for his critical review of this paper and permission to report the case, which was his private patient.

REFERENCES

1. Hare, M. L. C.: Tyramide Oxidase. I. A New Enzyme System in Liver. *Biochem. J.*, 22:968-79, 1928.
2. Blaschko, H.: Amine Oxidase and Amine Metabolism. *Pharmacol. Rev.*, 4:415-458, 1952.
3. Blaschko, H., and Philpot, Flora J.: Enzymatic Oxidation of Tryptamine Derivatives. *J. of Physiol.*, 122:403-407, 1953.
4. Sjoerdsma, A., Smith, T. E., Stevenson, T. D., and Udenfriend, S.: Metabolism of 5-Hydroxytryptamine (Serotonin) by Monoamine Oxidase. *Proc. Soc. Exper. Biol. and Med.*, 89:36-38, 1955.
5. Blaschko, H., Richter, D., and Schlossmann, H.: The Inactivation of Adrenalin. *J. Physiol.*, 90:1-17, 1937.
6. Schayer, Richard W., Smiley, K., Davis, Jane, and Kohayashi, Yutaka: Role of Monoamine Oxidase in Nor-Adrenaline Metabolism. *Am. J. Physiol.*, 182:215-286, 1955.
7. Bogdanski, D. F., and Udenfriend, S.: Serotonin and Monoamine Oxidase in Brain. *J. Physiol. and Exper. Therap.*, 116:7-8, 1956.
8. Zeller, E. A., Barsky, J., Fouts, J. R., Kircheimer, W. F., and Van Orden, L. S.: Influence of Isonicotinic Acid Hydrazide (INH) and 1-isonicotinyl-2-isopropyl hydrazide (IIH) on Bacterial and Mammalian Enzymes. *Experientia*, 8: 349-350, 1950.
9. Randell, Lowell O., and Bagdon, Robert E.: Pharmacology of Iproniazid and Other Amine Oxidase Inhibitors. *Ann. N. Y. Acad. Sci.*, 80: 626-639, 1959.
10. Horita, Akira: Pharmacology of JB-516 (PIH). *Ann. N. Y. Acad. Sci.*, 80:590-96, 1959.
11. Zeller, E. A.: Enzymologic Effects of Marsilid and Related Hydrazine Derivatives. *J. Clin. and Exper. Psychopath. and Quart. Rev. of Psy. and Neurolog.*, 19:27132 (Supp. 1), 1958.
12. Shore, P. A.: Possible Mechanism of Antidepressant Action of Marsilid. *J. Clin. and Exper. Psychopath. and Quart. Rev. of Psych. and Neurolog.*, 19 (Supp. 1): 56-60, 1958.
13. Zeller, E. A., and Barsky, J.: *In Vivo* Inhibition of Liver and Brain Monoamine Oxidase by 1-isonicotinyl-2-isopropylhydrazide. *Proc. Soc. Exper. Biol. and Med.*, R1:459-461, 1952.
14. Chessin, Max, Dubnick, Bernard, Leeson, Gerald, and Scott, Charles C.: Biochemical and Pharmacological Studies of B-phenylethylhydrazine and Selected Related Compounds. *Ann. N. Y. Acad. Sci.*, 80:597-608, 1959.
15. Schayer, R. W.: *In Vivo* Inhibition of Monoamine Oxidase Studied with Radioactive Tyramine. *Proc. Soc. Exper. Bid. and Med.*, 84:60, 1953.
16. Corne, S. J., and Graham, J. D. F.: The Effect of Inhibition of Amine Oxidase *In Vivo* on Administered Adrenaline, Noradrenaline, Tyramine, and Serotonin. *J. Physiol.*, 135:339-349, 1957.
17. Carlsson, A.: 3, 4-Dihydroxyphenylalanine and 5-Hydrozytryptamine as Reserpine Antagonists. *Nature*, 180:1200, 1957.
18. Griesmer, E. C., Barsky, J. Dragstedt, C. A., Wells, J. A., and Zeller, E. A.: Potentiating Effect of Iproniazid on the Pharmacological Action of Sympathomimetic Amines. *Proc. Soc. Exper. Biol. and Med.*, 84:699-700, 1953.
19. Udenfriend, S., Weissbach, H., and Bagdanski, D. F.: Increase in Tissue Serotonin Following Administration of Its Precursor 5-hydroxytryptamine. *J. Biol. Chem.*, 224:803-810, 1957.
20. Bogdanski, D. F., Weissbach, H., and Udenfriend, S.: Pharmacological Studies with the Serotonin Precursor 5-hydroxytryptamine. *J. Pharmacol. Exptl. Therap.*, 122:182, 1958.
21. Fouts, J. R., and Brodie, B. B.: On the Mechanism of Drug Potentiation by Iproniazid. *J. Pharmacol. Exptl. Therap.*, 116:480-485, 1956.
22. Goodman and Gilman: "The Pharmacological Basis of Therapeutics. 2nd Edition, 1955, p. 490.
23. Davis, Wm. A.: History of Marsilid. *J. Clin. and Exptl. Psychopath. and Quart. Rev. of Psych. and Neurolog.*, 19 (Supp. 1): 1-4, 1958.
24. Scherbel, Arthur L.: Clinical Experience in Treatment of Over 2000 Cases with Amine Oxidase Inhibitors. *Dis. of Nerv. Syst.*, 21 (Suppl. X): 67-69, March 1960.
25. Dunlop, Edwin: Depression: Treatment of Office Patients with Phenelzine (Nardil). *Rhode Island Med. J.*, 42:656-658, 1960.
26. Saunders, J. S., Roukema, R. W., Kline, N. S., and Bailey, S. d'A.: Clinical Results with Phenelzine. *Am. J. Psych.*, 116:71, 1959.
27. Sainz, Anthony: The Phenopraxic Activity of a Nonnoxious Antidepressant. *Ann. N. Y. Acad. Sci.*, 80:780-789, 1959.
28. Sainz, Anthony: Diagnosis and Treatment of Endogenous Depressions with Monoamine Oxidase Inhibitors. *Dis. Nerv. Syst.*, 20:537, 1959.
29. Susbac, H. Egon, and Genauer, Mortimer B.: Anesthesia Techniques for Excisional Pulmonary Surgery; Experiences with Iproniazid. *Quart. Bull. Sea View Hosp.*, 14:110-126.
30. Singh, Harbhajan: Atropine-like Poisoning Due to Tranquilizing Agents. *Am. J. Psychiat.*, 117: 360-361, 1960.
31. O'Reilly, P. O.: Phenelzine Dihydrogen Sulfate Intoxication. *Canad. Med. Assn. J.*, 82:928-930, 1960.

Eastern Psychiatric Research Association

(QUARTERLY MEETING—JUNE 22, 1961)

An Organization of Ex-Patients of a Psychiatric Hospital

(Twenty-five Years of Service)

JACOB H. FRIEDMAN, M.D.*

In 1939 the author[1] described the first organization in the United States of ex-patients of a psychiatric hospital. This organization was founded in December 1934 by a group of ex-patients of the Hastings Hillside Hospital, Hastings-on-Hudson, New York, a 41-bed charitable psychiatric hospital. The 30 charter members chose the name, "The Wender Welfare League," for Dr. Louis Wender, "in honor of the director of the hospital who was responsible for our recovery." To be a member of the Wender Welfare League was considered an honor. Membership in the organization was open to ex-patients and their immediate relatives. However, a few doctors, nurses, an occupational therapist and members of the office staff who had very close contact with the patients, became members by invitation. The preamble of the constitution read: "The purpose of the Wender Welfare League shall be to promote the welfare of the Hastings Hillside Hospital; to aid in the continuance and extension of the humane work for the relief and care of mental illness; to assist those who were formerly patients in the hospital or who, having had members of their immediate families as patients, have a common basis for joining in a movement to promote mental health."

In April 1936 the League secured a State charter, changing its name to the League for Mental Health, Inc. At that time there was a membership of 300 covering a wide range, economically and socially, similar to the patient population at the hospital, such as a Ph.D., professional people, artisans, marginal wage earners, shop keepers and artists. They were held together by their common experience and interest in the work. There were regular monthly meetings in mid-town New York City and about 150 members would attend a meeting which was partly devoted to business, followed by entertainment and refreshments. A four page bulletin was published. The League promoted a program of useful activity, adapted to the needs of the hospital and its patients, arranging bi-weekly entertainment and refreshments for the patients. At these hospital functions these recovered patients served as a source of encouragement to those undergoing hospitalization. An annual field day was held at the hospital during which patients and ex-patients competed in games. The members of the League had an intimate knowledge of the hospital and its needs, and thus the money raised was spent wisely in providing additional hospital facilities and comforts. Many discharged patients became members of the League and found a hearty reception in the group. In it there was some medium for social expression. In many instances discharged patients reported that the League helped tide them over the difficult period when they found themselves alienated from former friends and former interests.

The question arose as to what prompted ex-patients in 1934 to conceive and carry out this type of organization which was a radical idea at the time. I believe it was accomplished because the hospital had only 41 beds and it was conducted along simple lines. Financial and social status afforded the patient no advantage, payments varying from nothing to a moderate fee. There were few paid employees outside the professional staff. Each patient was required to assume responsibility when able to undertake it. It was a stigma to be idle. A lawyer was eager to chop wood as did a fellow patient who had performed manual work. This common participation in menial but necessary tasks tended to eliminate snobbish or superior attitudes and made the patients face fundamentals. There was intimate contact between staff members and patients. In addition to individual psychotherapy, group psychotherapy was also given. They met, not as strangers, but as friends who lived and worked together, and at these sessions their more intimate problems were worked through in a group. Thus besides having a deeper understanding and acceptance of their own problems they also were given a perspective and a less shrinking attitude towards the entire subject of mental illness.

Throughout twenty-five years, as an invited member from its inception, I have been able to observe how these peoples' attitudes have been affected permanently. The existence of this League of ex-patients marked a milestone in the progress of mental hygiene. It was the first organization in this country of ex-patients of a psychiatric hospital. The organization helped the adjustment of the discharged patient through the difficult transitional period when he needed to fully recover his normal

*Director of Neuropsychiatric Service, Fordham Hospital, Bronx, N. Y.; Director of Mental Hygiene Clinic, Lebanon Hospital, Bronx, N. Y.

standing in society by receiving encouragement and sympathetic companionship. Furthermore, through these person to person contacts, each patient was an active participant in allaying the stigma of having had a mental illness.

There are now a number of organizations of ex-patients of psychiatric hospitals and their friends among which may be mentioned, Recovery Incorporated, Fountain House, Rockland Hospital Guild, and the Manhattan State Hospital Guild.

In 1939 the Hastings Hillside Hospital moved its quarters to Glen Oaks, Long Island, and the name was changed to Hillside Hospital. Dr. Louis Wender, the first Medical Director of Hastings Hillside Hospital and of Hillside Hospital, resigned as Medical Director in 1943. Later the Bridge (Hilda and Israel Strauss League) was organized at the Hillside Hospital. This latter organization has a social worker and other workers provided by the Hillside Hospital. It is an expense of the hospital to keep the organization. Other organizations of ex-patients of psychiatric hspitals, give to their members but the members give little in return. I am not deriding other organizations of ex-patients of psychiatric hospitals which are subsidized, since these organizations are also essential in the reintegration of the patient after he leaves the hospital. I am indicating the uniqueness of the first organization of ex-patients of a psychiatric hospital.

Although not connected with Hillside Hospital, the League for Mental Health continued its activities and the members remained loyal to the League, continuing to function, always keeping in view its purpose as noted in the preamble of the constitution: "to aid in the continuance and extension of the humane work for the relief and care of mental illness." In 1944 it initiated the first evening mental health clinic at the Beth Israel Hospital, New York City, enabling people of low economic status to obtain help while continuing their daily work. In 1945 it created a hospitalization fund which subsidized private institutional psychiatric care for people who required intensive and individual treatment available only in costly private hospitals. Such treatment was also not available at that time in state-supported institutions or general hospitals with psychiatric units. In 1952 it operated a subsidized psychotherapy plan and consultation service. A selected group of patients received treatment from a panel of psychiatrists at a minimum fee, one-half of which was paid by the patient and one-half by the League. The patients continued with their normal occupations and were treated in the offices of these psychiatrists. In 1956 it established the "Dr. Louis Wender Psychophysiologic Research Laboratory" at the Abraham Jacobi Hospital, associated with the Albert Einstein College of Medicine. Recently the League initiated a Psychiatric Research Laboratory at the Psychiatric Department of the Hadassah Medical School, Hebrew University in Israel.

In 1941 the League for Mental Health changed its constitution so that those interested in the field of mental health could join its organization. There is a present membership of over five hundred. Although a number of the original members have died, the main work of the organization is still carried on by the group of early members. The League has always depended on membership dues and financed its projects chiefly through contributions from members and fund-raising activities. It is not subsidized by any individual or foundation. Volunteers do all the work. There are no salaried employees or paid activities. The only operating costs are printing, mailing, office rent and meeting room expenses.

What has prompted these ex-patients to keep the League functioning and why has the League for Mental Health remained fuctioning for the past 25 years without any subsidies whatsoever? At the Hillside Hospital, Hastings-on-Hudson, there prevailed a non-favoritism and democratic milieu plus the loyalty and enthusiasm of the entire hospital staff, ranging from the kitchen help, gardener, attendants, nurses, occupational therapist, social worker and residents, to the Director. The Director, Dr. Louis Wender, gave himself fully to the patients, and even made rounds as late as 9:00 or 10:00 P.M. He represented the good omnipotent father. In addition, individual and group psychotherapy played a prominent role. In individual psychotherapy the patient was made aware of his unconscious conflicts, his unwarranted and/or inadequate hostile behavior and/or his helpless dependent attitude with sexual immaturity from unresolved infantile conflicts and aspirations. The dynamics of group psychotherapy[2,3] through intellectualization, patient-to-patient transference, catharsis and group interaction, helped the patients to understand family group living and working out the early infantile frustrations and inadequacies. A positive group transference was established similar to the positive transference in individual psychotherapy. Although treatment is successful and the ex-patient is said to have worked through his transference situation, being symptom free and functioning in a normal manner, yet a vestige of a positive transference always remains. The former patient will speak highly of his psychiatrist and recommend others to him. If any difficult situation may arise he may telephone the psychiatrist months to years after therapy had been terminated, to ask for advice. Such individual positive transference, which I believe can last for a lifetime, also occurs in groups. This phenomenon has occurred with the League for Mental Health. Thus with individual psychotherapy, group psychotherapy and the milieu of the 41-bed hospital, the patients became independent and mature, learning to live and give rather than receive and demand. These patients, with no grudge, no resentment and no repressed hostilities, became mature and are able to express their

ego strivings and obtain libidinal satisfaction by giving instead of taking. These ex-patients have remained active in the League because they advanced to maturity at Hastings Hillside Hospital, and with the vestiges of a positive transference, persisted in their loyalty to the League these 25 years.

Summary and Conclusion

(1) The activities for 25 years of the first organization of ex-patients of a psychiatric hospital and the psychodynamics are described.

(2) Private psychiatric hospitals and state hospitals should emulate Hastings Hillside Hospital in their follow-up club or ex-patients' organization so that the dependent ex-patient can become independent, outgoing, and giving instead of receiving.

1749 Grand Concourse, New York 53, N. Y.

REFERENCES

1. Friedman, J. H.: An Organization of Ex-Patients of a Psychiatric Hospital. *Ment. Hyg.*, 23 (July 1939), 414-420.
2. Wender, L.: Dynamics of Group Psychotherapy and Its Application. *J. Nerv. and Ment. Dis.*, 84 (July 1936), 54-60.
3. Wender, L.: Group Psychotherapy: A Study of Its Application. *Psychiat. Quart.*, 14 (Oct. 1940), 708-18.

Discussion on Dr. Friedman's Paper

LOUIS WENDER, M.D.

To better understand how the Welfare League came into being, I shall try to elaborate the setting from which it stemmed. I was fortunate to have had the opportunity in 1927 to organize the Hastings Hillside Hospital for voluntary, borderline mental patients. The hospital was a pilot project and I was given a free hand to carry out my philosophy of therapy in a mental institution. Since this was a pilot project, no chronic psychotics or severely disturbed patients were admitted. The entire population consisted of borderline schizophrenics, mild depressions and severe psychoneurotics. Admissions were determined only by the suitability of the patient to respond to psychotherapy. Financial considerations were secondary. We had no investigators to look into financial means of the family. Rates varied from nothing to $25.00 a week. Treatment and assignments to rooms were determined by the patients' needs and not by what they paid. All patients were treated alike, irrespective of social or economic status. This afforded a real democracy within the hospital; the mixing of professional people, students, small business men, housewives etc. Nurses, occupational therapists, doctors and the director himself were all part of this community and not remote individuals. Patients were not numbers; they were treated as part of the social structure. The whole set-up stressed the worth of the individual—not verbally but consistently through attitudes and practices. They were made to think that they were part of the hospital and that the hospital was theirs. It was their home. Thus, they began to help with the cleaning and gardening, made objects for decoration of the hospital in occupational therapy, and were allowed to cook one day a week, even make up their own menu. This was in addition to arranging their own entertainment and publishing an intra-mural newspaper.

Our patients were not different from the borderline type admitted elsewhere. As is well known, neurotics are infantile, demanding and when their demands are not met, they feel frustrated. They are the people who, on the outside, feel they did not get enough satisfaction, felt frustrated and introjected the libido upon themselves.

Through individual therapy but more through group psychotherapy, which I started in the early 30's, the entire running of the hospital became geared to engender in the individual patient a sense of being a person accepted by the group. It gave him a place in this little community where he had been rejected on the outside. As a matter of fact, one of the ideas of group psychotherapy which I have evolved over the years is based on the proposition that the individual in his early life has not been able to express himself in the small group (the family); that he is rejected by the family and thus the feelings of frustration and insecurity started, he introjected his libido upon himself. In Hastings Hillside we endeavored to relieve the patient of his old fixations and feelings of rejection. Here the patient found himself accepted, able to express himself without being punished. Then his ego development started. He began to learn to extrovert and give of himself instead of being the infant-demanding and taking.

The idea of an ex-patient organization was conceived by a few discharged and recovered patients. At first they visited the hospital, provided entertainment, games and, as finances permitted, purchased furniture for the old hospital. The spirit of this group became stronger with the result that most of the patients who left Hillside Hospital asked to join the League, not only for the purpose of seeing their old friends, but for the spirit of giving of themselves to a cause in which they felt very important. As the group grew, it began to meet regularly on the outside and its activities spread in various directions. At one time, not only did the members help patients recently discharged with rehabilitation through companionship, but also with loans to carry them over until they could obtain employment. They established a Thrift Shop to rehabilitate patients not working for the first few months, to get them out into the world of reality.

Members of the staff were invited to the meetings, but the initiative remained in the hands of the ex-patients. The accomplishments of the League

in the past 25 years include the establishing of a loan fund, a revolving hospitalization fund, subsidizing psychiatric care by the private physician with the patient choosing his own psychiatrist, and a gift of $10,000.00 to the Hillside Hospital for a playground. At present, the League has gone out into other ventures in establishing a psycho-physiological laboratory at the Albert Einstein Medical School and recently a research fellowship in the Hadassah Medical School in Israel.

The League members, people of modest means and many of them with limited educational background are pioneers in the field of psychiatric aftercare. Now there are many similar organizations, sponsored by professionals in the field, or by civic-minded members in the community. Now, Hillside has an organization called "The Bridge." There is also the Fountain House and a number of less well-known projects. But the League still retains the distinction of being the oldest organization in the field: an entirely self-financed, self-directed enterprise of former patients and their relatives, who, through their own positive experience, have sought to enable others to find themselves.

The following are abstracts of the other papers read at the meeting. These papers will be reported in full in subsequent issues of *Diseases of the Nervous System*

Ambulatory Maintenance by Electrocoma Therapy

Ten Year Follow-up of Fifty Patients Treated in a Private Office

EMERICK FRIEDMAN, M.D.

In accordance with the developing philosophy of extramural care of mental illnesses a program of maintenance therapy was conducted under office conditions. Fifty patients, suffering from classical psychoses or disabling psychoneurosis, were treated and studied for an average of ten years. Their previous histories had shown repeated hospitalizations and continued invalidism for years. Modalities of electrotherapy were administered intensively for several weeks and then gradually tapered off in frequency while psychotherapy was given.

By establishing a proper therapeutic locale in a private office, and by developing rapport with patients and their families, a background of protectiveness and tolerance could be established. Understanding of problems by the patient and family developed as well as recognition of premonitory reactions. Ready accessibility of the therapist at these times for psychotherapy, electrocoma, or indicated combinations thereof was an important factor. A certain, almost periodic, build-up of tensions was frequently encountered and could be prevented by suggestions or somatic measures. In this manner of ambulatory therapy these patients were maintained on satisfactory and productive vocational, social and marital levels despite poor prognosis and prior histories of hospitalizations and continued invalidism.

Attending Psychiatrist, Memorial Hospital, Albany, N. Y., and Acting Chief Consultant, Marshall's Sanitarium, Troy, N. Y.

American Psychiatry

Current Practices and Views in Psychopharmacology

BRIAN C. CAMPDEN-MAIN, M.D., and
THELMA J. CAMPDEN-MAIN

The data reported in this paper are based on responses to a mail survey conducted by the authors in May 1960 of members of the American Psychiatric Association. This paper discusses the psychiatrist's attitudes and views towards psychopharmacology, the relationship between his attitudes and his practices, and the medications or combinations of medications that he prescribes.

Psychotherapy is clearly the commonest therapeutic approach, being used by 98% of the survey respondents. Psychopharmacotherapy is the second commonest procedure: 82% of the respondents report using tranquilizers and 72% using antidepressants. Sedatives were used by 53% and other drugs by 39%. Between 60 and 65% indicate that they rarely use group psychotherapy, psychoanalysis or EST. The authors discuss and interpret these and other findings in detail.

A complete statistical description of the sample is given.

Parenteral Niamid in Depressions

H. BECKETT LANG, M.B., F.A.C.P.

This is a preliminary report on the use of Parenteral Niamid in patients with depressive reactions.

The method of treatment was intravenous using 2.5% glucose in 1000 cc. 45% normal saline as the vehicle at the rate of 500 cc. per hour. The Niamid dosage was 250 mg. in 20 cc. distilled water. One case received 500 mg. in 20 cc. distilled water. Administration was by low Y intravenous tube. The rate of Niamid solution was 2 cc. per minute.

Blood pressures were recorded before intravenous, at the start of Niamid injection, then every 2½ minutes until completion, then every 15 minutes until completion of intravenous solution.

Patient selection was based on 1) failure to respond to high oral dosage, 2) previous treatment with electroconvulsive treatment and moderate response with relapse, and 3) refusal to accept electroconvulsive therapy.

Diagnoses were neurotic depressive reactions, manic depressive, depressed and schizo-affective depressions.

Patients must remain in bed until blood pressure has returned to normal. Paradoxical rises can occur but a hypotensive reaction within five minutes after the Niamid injection is the usual finding.

Side reactions consisted of two severe orthostatic hypotensive reactions, two transient oedemas of feet and two transient febrile reactions. Parkinsonism, akathisia or dystonia did not occur. In one case SGOT rose to 62 units but was normal on discharge.

All 16 patients, 13 females, 3 males showed "reversal" of their depressive reaction within five to six day. The schizo-affective patient required supplementary electroconvulsive treatment because of persistent delusions. One patient, after three intravenous treatments, had to be changed to intramuscular because of difficult veins.

Based on present observations, Parenteral Niamid, intravenous or intramuscular, provides another modality of therapy for depressive reactions but does not replace electroconvulsive therapy. This study is being continued.

Book Reviews

DISEASES OF THE INTERVERTEBRAL DISC. Reuben Rabinovitch, B.A., M.Sc., M.D. Charles C. Thomas, Springfield, Illinois, 1961. 152 pp. $8.50.

This monograph was written in an attempt to find evidence for the hypothesis that "some systemic disease of connective tissue structures in general and of disc cartilage in particular may be the true cause for multiple alterations, both in discs and in their adjacent ligamentous and bony structures," since mechanistic interpretations have been often insufficient to explain these. The author presents among others case histories of four patients (two with post-morted control) with changes at almost all disc levels, where no causal agent could be found. He speculates on possible metabolic and infectious conditions as possible important factors.

Experimental work with monkeys is reported; pathological findings (including biochemical and physiochemical changes) offer valuable criteria for further research.

Of clinical importance is author's description of the foramen intervertebrale, with the changing relationships at different levels between the nervo-root anchorage zones and the posterolateral tip of the disc. He prefers and suggests the concept of an interpeduncular canal rather than intervertebral foramen. The book contains a short analysis of literature on the pathogenesis of disc disease.

For summary, it provcs merely the necessity for further investigative work, and outlines some of the criteria and possible methods.

Although interesting in this regard, it leaves the reader somewhat disappointed, since more elaborations as to the causal relationships with systemic disease were expected and only speculations offered.

Cornelius Boelhouwer, M.D.

MEANING AND METHODS OF DIAGNOSIS IN CLINICAL PSYCHIATRY. Thomas A. Loftus, M.D. Philadelphia: Lea & Febiger, 1960. 169 pages. $5.00.

This is a different and extremely valuable contribution. It is unique in that it stresses a sharpening of diagnostic acumen rather than merely furnishing descriptions of symptoms. It should be of particular value to the generalist or non-psychiatrist who seeks a firm foothold in psychopathology and is not too concerned with the different schools of psychiatric thought. Speculation and theorizing are held to the barest minimum.

A most valuable portion of the book is devoted to comparative case histories, where the diagnostic entities are charted side by side in tabular form. Another valuable section is the one on history-taking. The author cites many examples where the wording of one's questions makes for vast differences in the patient's responses.

An interesting chapter is devoted to the various levels of cooperation of the patient. Ranging from the need for magic, to the parentifying level up to the self-reliant stage, the author provides examples of each in the patient's attitude, thinking and behavior. This information, if assimilated, should enable the physician to understand and cope with some of the demands of difficult patients.

Wilfred Dorfman, M.D.

BALDPATE, Inc.

Geo. Fleetwood 2-2131 **Georgetown, Mass.**

Located in the hills of Essex County, 30 miles north of Boston

For the treatment of
psychoneuroses, personality disorders, psychoses, alcoholism and drug addiction.
Definitive psychotherapy, somatic therapies, pharmacotherapy. Milieu-therapy under direction of trained occupational and recreational therapists.

Accredited by Joint Commission on Accreditation of Hospitals

HARRY C. SOLOMON, M.D.
Consulting Psychiatrist

PATRICK J. QUIRKE, M.D.
Medical Superintendent

FAIRVIEW Sanitarium

2928 S. PRAIRIE AVE.
CHICAGO
Phone Victory 2-1650
J. DENNIS FREUND, M.D.
Medical Director

DEVOTED TO THE ACTIVE TREATMENT OF

MENTAL and NERVOUS DISORDERS

Specializing in Psycho-Therapy, and Physiological therapies including:

- Insulin Shock
- Electro-Shock
- Electro-Narcosis
- Out Patient Shock Therapy Available

ALCOHOLISM Treated by Comprehensive Medical-Psychiatric Methods.

BEVERLY HILLS CLINIC and SANITARIUM

210 N. Westmoreland Avenue **WHitehall 3-4651**

Dallas 11, Texas

A private clinic and hospital for nervous and mental diseases both for in-patients and out-patients —stressing a homelike environment with separate building units and special cottages—air-conditioned.

A complete neuropsychiatric diagnostic and treatment center including a department of psychology—encephalography—clinical laboratory and X-ray—psychotherapy—electroshock and insulin coma therapy, as well as psycho-surgery.

ARTHUR J. SCHWENKENBERG, M.D.
JOSEPH L. KNAPP, M.D.
JACKSON H. SPEEGLE, M.D.
Neurology

FRED H. JORDAN, M.D.
HENRY P. HARE, JR., M.D.
LUDLOW M. PENCE, M.D.
Psychiatry

A NEUROPSYCHIATRIC FOUNDATION
THE

ROGERS MEMORIAL HOSPITAL

The Hospital is situated on the Nashotah Lakes, 30 miles west of Milwaukee, providing the ideal, restful country environment and the facilities for the modern methods of therapy of psychoneuroses, psychosomatic disorders, alcoholism, and the other neurologic and psychiatric problems. Occupational therapy and recreational activities directed by trained personnel.

OCONOMOWOC, WISCONSIN
PHONE LOGAN 7-5535

EUGENE FRANK, M.D.
WILLIAM C. JANSSEN
LOREN J. DRISCOLL, M.D.

OWEN OTTO, M.D.
Medical Director

LEROY A. WAUCK, PH.D.
Clinical Psychologist
JOSEF A. KINDWALL, M.D.
Consultant

FAIR OAKS

INCORPORATED

SUMMIT, NEW JERSEY

A fully approved Hospital for intensive treatment and management of problems in Neuropsychiatry

OSCAR ROZETT, M.D.
Medical Director

THOMAS R. PROUT, JR.
Administrator

50 BEDS **HILLCREST HOSPITAL** **EST. 1905**

(formerly The Retreat, Inc.)
DES MOINES 12, IOWA

For the diagnosis and treatment of Nervous and Mental Disorders in a homelike environment.

Occupational Therapy, Physiotherapy and Shock Therapy
Open Psychiatric Staff

HERBERT C. MERILLAT, M.D., *Medical Director* HERBERT W. VETTER, *Administrator*

PINEWOOD **Dr. Joseph Epstein, F.A.P.A.**
Dr. Louis Wender, F.A.P.A. **Physicians in Charge**

DR. WALTER A. THOMPSON, F.A.P.A., Clinical Director

Westchester County - Route 100 - Katonah, N. Y. - Tel.: Central 2-3155

A competent sixty bed hospital, psychoanalytically oriented but using multi-disciplinary approach. Patients admitted for "short-term" therapy or more prolonged study. Additional facilities for O.P.D., Day Center Therapy and consultation. Weekly clinical conferences open to the profession. A.P.A. members may receive staff privileges and treat their own patients.

New York City Offices

DR. EPSTEIN—975 Park Ave.—Tues., Thurs., Sat. RH 4-3700

DR. WENDER—59 East 79th St.—Mon., Wed., Fri. BU 8-0580

Saint Joseph Sanitarium

(Supervision of Sisters of Mercy)

P. O. BOX 236 — DUBUQUE, IOWA

or phone 3-8291 for information

Mild Mental and Nervous Cases
also
Convalescent and Rest Patients

Shock Therapy, Hydrotherapy, Physiotherapy, Occupational Therapy. Competent Staff.

SANITARIA DIRECTORY

The institutions listed below are among the finest private sanitaria in the United States. They offer private, individual specialized care to the patient.

BALDPATE, INC.
GEORGETOWN, MASSACHUSETTS

BEVERLY HILLS CLINIC AND SANITARIUM
DALLAS 11, TEXAS

ELMLAWN (The Wilgus Sanitarium)
ROCKFORD, ILLINOIS

FAIR OAKS
SUMMIT, NEW JERSEY

FAIRVIEW SANITARIUM
CHICAGO, ILLINOIS

FOREST SANITARIUM
DES PLAINES, ILLINOIS

GLENSIDE
BOSTON 30, MASSACHUSETTS

HALL-BROOKE
GREEN FARMS, CONN.

HILLCREST HOSPITAL
(formerly The Retreat, Inc.)
DES MOINES 12, IOWA

PINEWOOD
KATONAH, NEW YORK

RING SANATORIUM
ARLINGTON, MASSACHUSETTS

ROGERS MEMORIAL HOSPITAL
OCONOMOWOC, WISCONSIN

ST. CLAIR HOSPITAL
DETROIT 14, MICHIGAN

ST. JOSEPH SANITARIUM
DUBUQUE, IOWA

Calms the Tense, Nervous Patient

in anxiety and depression

The outstanding effectiveness and safety with which Miltown calms tension and nervousness has been clinically authenticated by thousands of physicians during the past six years. This, undoubtedly, is one reason why meprobamate is still the most widely prescribed tranquilizer in the world.

Its response is predictable. It will not produce unpleasant surprises for either the patient or the physician. Small wonder that many physicians have awarded Miltown the status of a proven, dependable friend.

Miltown®

meprobamate (Wallace)

Usual dosage: One or two 400 mg. tablets t.i.d.
Supplied: 400 mg. scored tablets, 200 mg. sugar-coated tablets; bottles of 50. Also as MEPROTABS®—400 mg. *unmarked*, coated tablets; and in *sustained-release* capsules as MEPROSPAN®-400 and MEPROSPAN®-200 (containing respectively 400 mg. and 200 mg. meprobamate).

WALLACE LABORATORIES
Cranbury, N. J.

CM-5642

Clinically proven in over 750 published studies

1. Acts dependably — without causing ataxia or altering sexual function
2. Does not produce Parkinson-like symptoms, liver damage or agranulocytosis
3. Does not muddle the mind or affect normal behavior